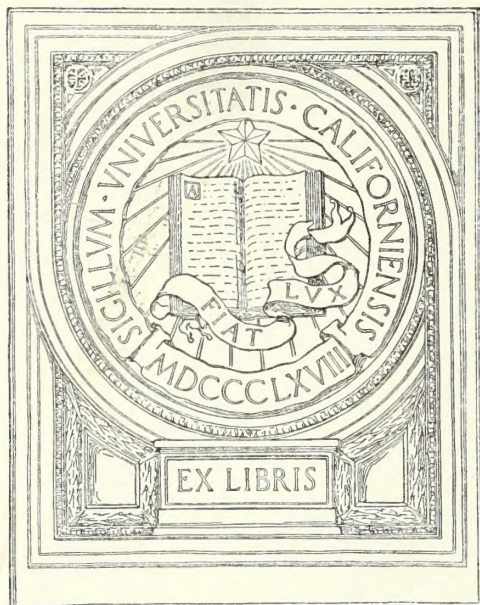


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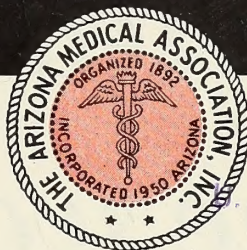
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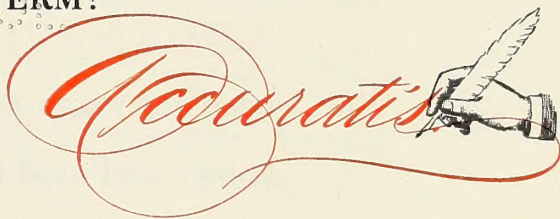


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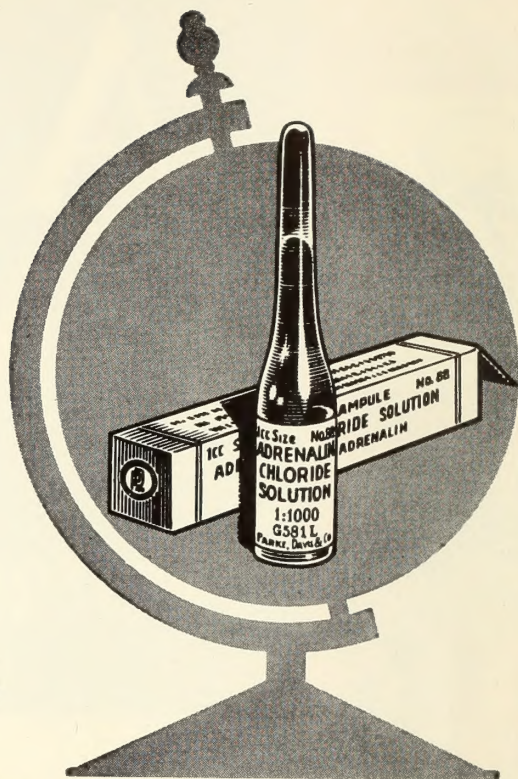
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(1) Schweigert B. S.: Significance of Vitamin B₁₂ and Related Factors, *J. Am. Dietetic Assoc.* 26:782 (Oct.) 1950.

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The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.



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ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 1



JANUARY, 1951

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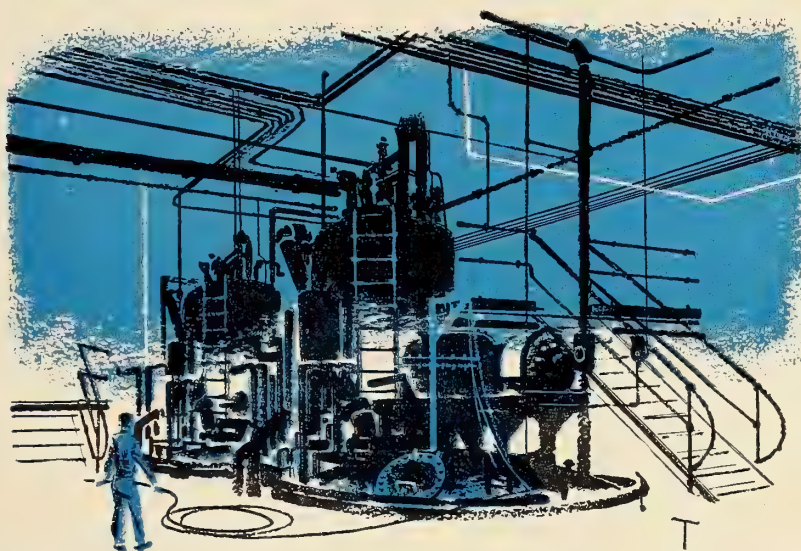
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*Pitt, C.K.: *The Art and Science of Artificial Infant Feeding*, J.M. Asso. Ala. 19:101 (Oct.) 1949.

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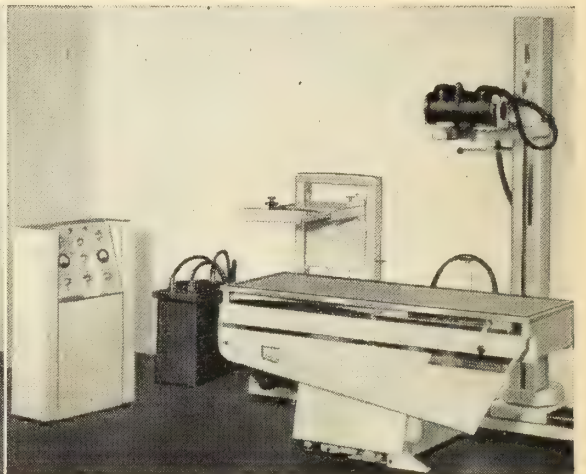
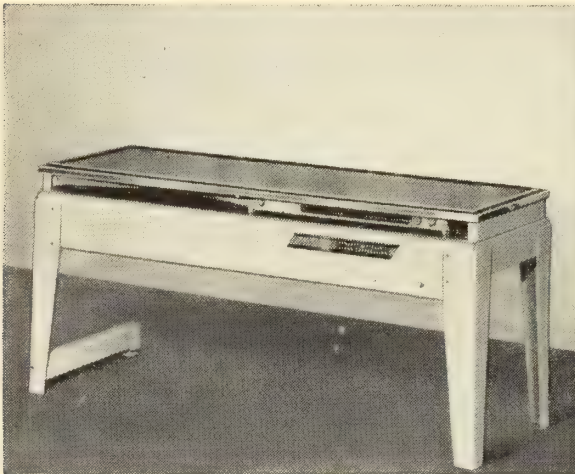
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7. People's League of Health: J. Lancet, 2:10, 1942.

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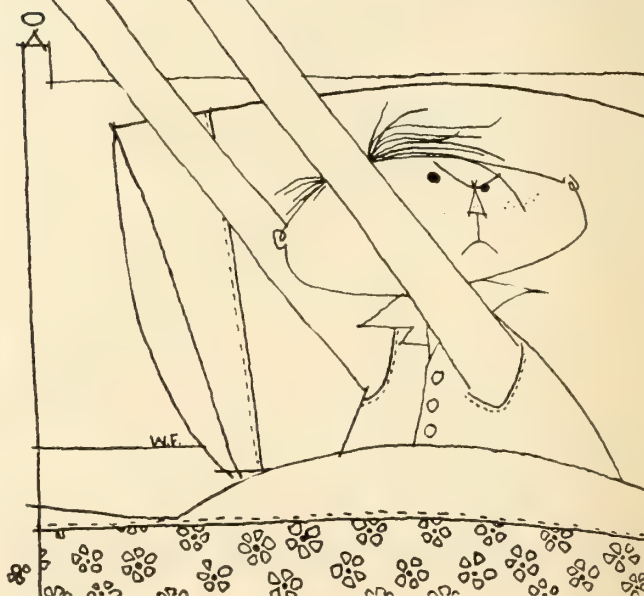
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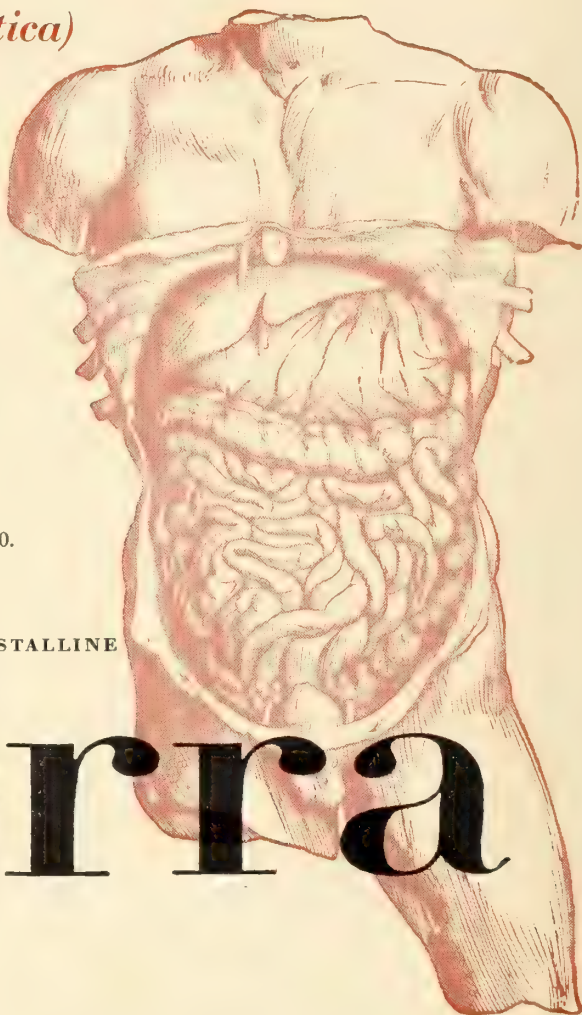
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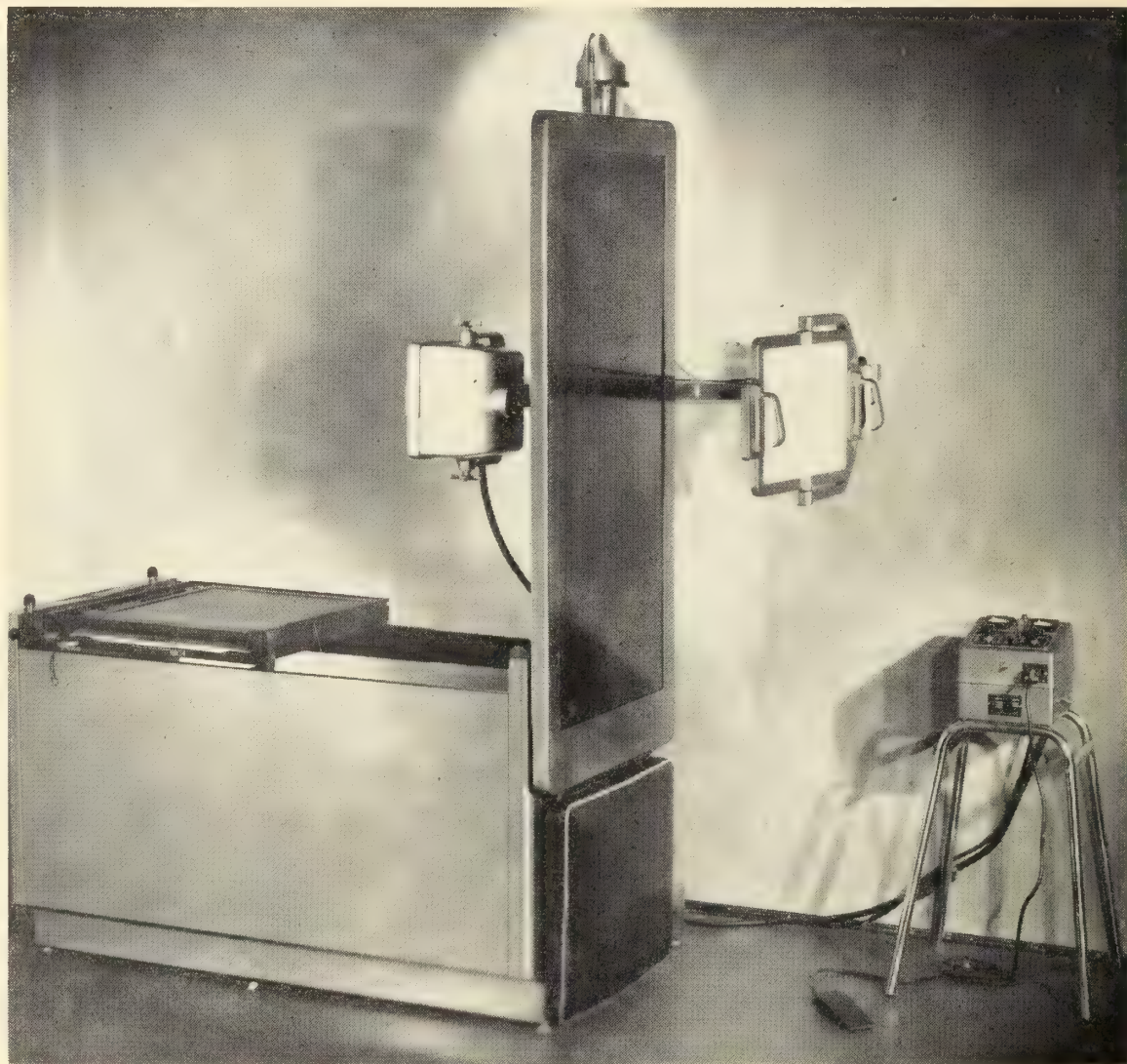
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Journal of ARIZONA MEDICAL ASSOCIATION

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*DIAGNOSIS OF POLIOMYELITIS

By

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INTRODUCTION

The prime purpose of this paper is to discuss the diagnosis of poliomyelitis in patients admitted to the Colorado General Hospital during the epidemic of 1946. Three hundred and thirty-nine patients were admitted with a tentative diagnosis of poliomyelitis which was confirmed in 303.

Selection of Patients In 1946, 900 cases were reported to the Colorado State Department of Public Health, (1) the first case having been reported in February. The date of the first admission to Colorado General Hospital was June 26th, approximately one month after the epidemic had been recognized. Until mid-July the majority of patients admitted were adults, but thereafter added facilities permitted admission of patients regardless of age. The more severely ill patients from the outlying Colorado communities were given preference.

General Characteristics Poliomyelitis is a viral infection, epidemics of which occur during the warm months. Sporadic cases may occur throughout the year. The majority of evidence supports the theory of spread by direct contact with individuals harboring the virus. Involved in particular are the anterior horn cells of the spinal cord and motor nuclei of the brain. In addition, careful sectioning of autopsy specimens (2 a&b) in man shows involvement of the pre-central gyrus of the motor cortex and severe lesions of the reticular formation of the medulla. Frequently involved are: (1) the red nucleus; (2) substantia nigra; (3) olivary nucleus; (4) roof nuclei of the cerebellum; (5) vestibular nuclei; (6) internuncial neurones of spinal cord

and (7) the proprioceptive cells of the posterior ganglia.

TABLE I POLIOMYELITIS

Colorado General Hospital Patients—303

Clinical Types

1. "Abortive"	
2. Non-paralytic	14%
3. Encephalitic	
4. Paralytic	
a. Spinal	53%
b. Bulbar	7%
c. Bulbosplinal	25%
e. Encephalosplinal	1%
e. Encephalobulbosplinal	

The clinical classification given in Table I may be conveniently used. The term "abortive" denotes those cases which show mild systemic symptoms, are difficult to diagnose and are suspected only during epidemics. The incidence of this type is difficult to determine. In a study (3) of three separate communities without selection of the family from an original case, the average ratio of frank to "abortive" cases was found to be approximately one to five. The *non-paralytic type* includes those cases which are characterized by meningeal signs, e.g., stiff neck and back and positive Kernigs, without clinical paralysis. *Clinical paralysis* is stressed because autopsy studies on primates challenged with human polio virus have shown that approximately 30 per cent of motor neurons can be "destroyed, necrotic or chromatolysed" without apparent paralysis (4). In any single epidemic approximately 50 per cent of frank cases are of the non-paralytic variety (5). The *paralytic type* includes those cases in which paralysis is evi-

*Aided by a Grant from the National Foundation for Infantile Paralysis.

dent and is subdivided on the basis of sites involved, e.g., spinal, bulbar, bulbo-spinal, encephalospinal and encephalobulbospinal.

Of 303 patients admitted to Colorado General Hospital, there were 42 non-paralytic cases (14 per cent); 162 spinal cases (53 per cent); 21 bulbar case (seven per cent); 75 bulbo-spinal cases (25 per cent) and three encephalospinal cases (one per cent). No "abortives" were hospitalized. These hospitalized cases included a high percentage of bulbar and severely involved patients, because limited facilities for care prevented admission of non-paralytic cases. Although encephalitic varieties are included in the classification of types of poliomyelitis, only three patients could be so classified with any degree of certainty.

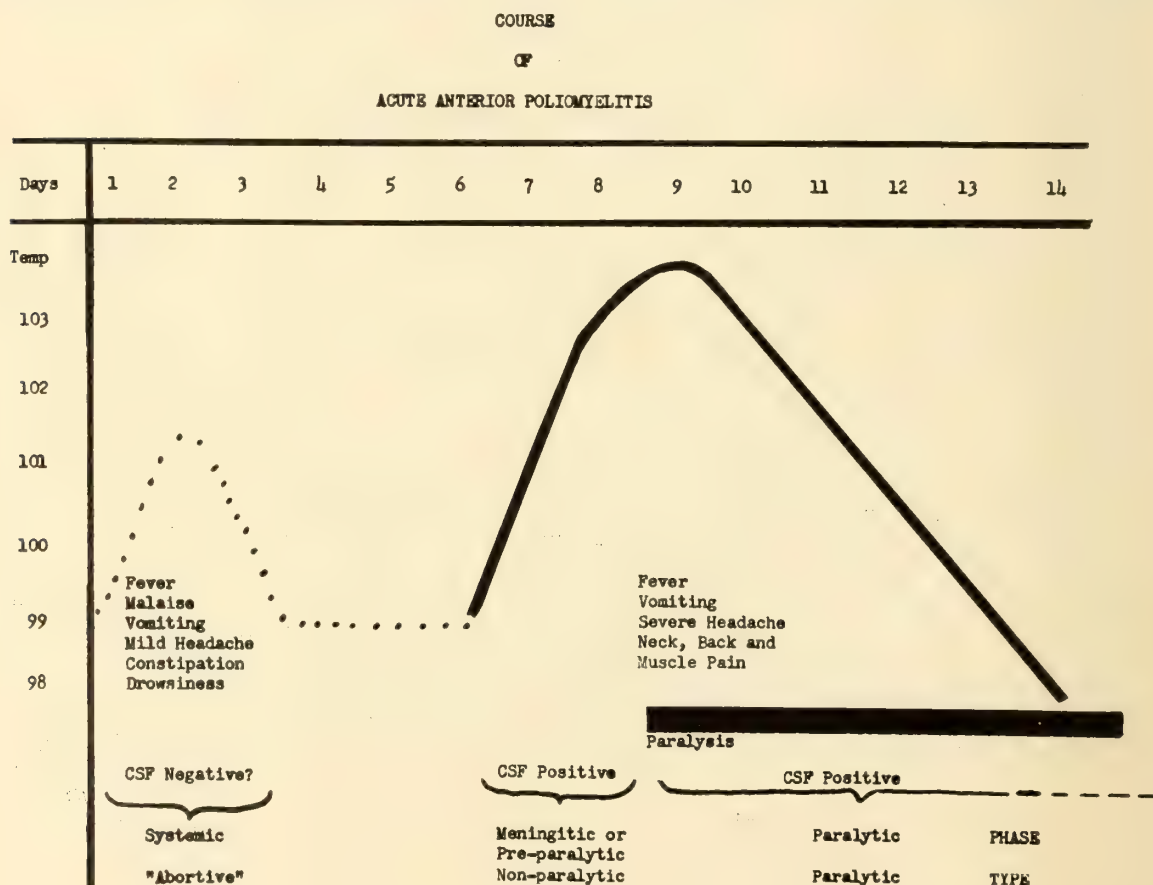
Poliomyelitis is a disease which seems to affect all age groups from the newborn to the elderly. Fronig (6) reports onset of symptoms in a four-day old infant and the writer has observed three patients in the seventh decade of life. In recent epidemics centered about large American cities the highest attack rate of recognized disease is in children under 15 years

of age with the greatest incidence occurring in the five-through nine-year age group (7). In spite of the previously mentioned selection of our cases, the highest incidence in this series still occurred in the five-to nine-year old children.

DIAGNOSIS

The clinical picture of poliomyelitis is extreme variable. Paralysis or weakness is characteristically spotty. The clinical course, as represented in Fig. 1, may be divided into three phases, e.g., *systemic* (symptoms of the "abortive case") *meningitic* or *pre-paralytic* and the *paralytic*. On the basis of previous studies (3, 8) one can expect that approximately 80 to 95 per cent of cases will not progress beyond the systemic phase and of the remaining individuals, about one-half will not develop clinical paralysis.

In a study (9) of 60 children who had intimate contact with cases of frank poliomyelitis and who had virus in the stool and/or elevated spinal fluid protein, symptoms of the "abortive" type of poliomyelitis were mild fever, headache, vomiting, constipation and drowsiness. Physical findings in this form of the disease are lacking



or minimal and consist of mild fever (99°-101°) and lethargy. Without virus studies such cases cannot be definitely diagnosed as poliomyelitis and are usually considered as suspects only during epidemics.

On careful questioning of patients with frank poliomyelitis one is likely to find that the majority have had prodromal symptoms (as those of the "abortive" case) several days before. Although symptoms of the systemic phase or the "abortive" type of disease are non-specific, evidence that the virus may be present in the central nervous system is suggested from studies by Andelman et al (10) and Bodian (11). In a group of contact children suspected of convalescing from sub-clinical poliomyelitis, 79 per cent of cases had spinal protein levels over 45 mg per cent, averaging 55 mg per cent, 11-45 days after onset of disease. (10) Should spinal punctures be done routinely during the period of acute symptoms on the "abortive" case, or prodromal period on the frank case, an increase in cells or elevation of protein level might be found. Although no studies are known in which the virus has been isolated from the central nervous system of "abortive" cases, in monkeys. Bodian (11) estimated that central nervous system lesions due to the virus appeared a day or less before onset of pre-paralytic symptoms. Characteristically in cases of frank disease, the systemic phase lasts one to three days and the patient is then symptomless for one to seven days. Accumulating evidence suggests that stress may be a determinant factor in the eventual course of the disease. In a series of 521 patients Top and Vaughan (12) found the incidence of stress or illness within 4 to 14 days of onset to be 35 per cent of patients who died, 20 per cent of all cases and 5 per cent of 497 case controls. A study by Russel (13) indicated a high incidence of severely paralytic disease in those patients who underwent undue stress a few days before or after onset of definite symptoms. In a study of 411 poliomyelitis patients from three epidemics, Horstmann observed that the degree of physical activity performed during the pre-paralytic phase "was associated with a significant increase in the incidence and severity of subsequent paralysis. Correspondingly, a significantly higher percentage of non-paralytic than paralytic patients gave a history of bed rest or minimal activity during the stages of the major illness" (14). A similar correlation has

been found in the chimpanzee by Levinson et al. (15) In a series of 261 patients admitted to Colorado General Hospital, 110 (42 per cent) gave a history of stress or injury, which they considered unusual, occurring within two weeks before onset. This study was not controlled and no attempt was made to correlate the severity of stress with degree of paralysis.

The *meningitic* or *pre-paralytic phase* is characterized by symptoms of frank disease, e.g., fever (99°-104°), severe headache, painful muscles in neck, back and legs, malaise and vomiting. In fairly large numbers of patients the disease will begin with symptoms of this phase.

Symptoms of the *paralytic phase*, to which approximately 50 per cent of cases progress in two to four days, are those of the pre-paralytic patient plus varied muscle paresis or paralysis. Temperature in the uncomplicated case returns to normal in two to seven days. Usually the maximal degree of paralysis will have developed by the time the temperature is normal, but an increase has been observed to occur after the febrile period in the third week in a rare case. Also a rare patient, infant or small child, may manifest nothing until onset of paralysis.

The wide range and incidence of individual symptoms of poliomyelitis can be appreciated from Tables II and III based on histories of 299 patients. The actual incidence of symptoms may be higher than represented because historical facts were sometimes incomplete. The most common symptoms were fever, headache, anorexia, nausea, vomiting and pain in the neck, back and legs.

Although only 18 per cent of the patients complained of constipation before entry, this symptom was almost invariably a problem on the ward. Two per cent of patients had mild diarrhea before admission. The incidence of sore throat was 17 per cent and this symptom occurred two and one-half times more frequently in the bulbar than in the spinal or non-paralytic case. Pohl (16) reports that in the Minnesota Epidemic of 1946 sore throat occurred ten times more often in the bulbar than in other cases. Abdominal pain, often associated with tenderness and muscle spasm, was a complaint in 11 per cent of patients. Urinary retention seemed to occur more frequently in young males with extensive involvement of the lower extremities. Cough (unassociated with bulbar or respiratory type of disease) and coryza were uncommon

manifestations. The symptoms of convulsions, unassociated with hypoxia, occurred very rarely. Shaking chills (five per cent) or chilliness (three per cent), common manifestations of acute infections, are relatively infrequent in this dis-

TABLE II
POLIOMYELITIS, COLORADO GENERAL
HOSPITAL, 1946
Common Symptomatology

Fever	91%	Mental confusion .	5%
Headache	64%	Pain in neck.....	47%
Anorexia	56%	Pain in back.....	46%
Nausea	50%	Pain in legs.....	30%
Vomiting	39%	Muscular aches	
Constipation	18%	and pains	15%
Diarrhea	2%	Abdominal pain ..	11%
Sore throat	17%	Urinary retention .	9%
Coryza	2%	Chills (shaking) .	5%
Cough	1%	Chilliness	3%
Drowsiness	14%	Paresthesias	4%
Malaise	12%	Hyperesthesia ...	3%
Fatigue	8%	Tremors	2%
Irritability	6%	Muscular twitching	1%

TABLE III
POLIOMYELITIS, COLORADO GENERAL
HOSPITAL, 1946
Bulbar Symptoms

Dysphagia	19%
Nasal speech	14%
Aphonia	1%
Weakness of voice.....	1%
Hoarseness	1%
Diplopia	4%
Blurring of vision.....	1%

TABLE IV
POLIOMYELITIS, COLORADO GENERAL
HOSPITAL, 1946
Cardinal Physical Signs

Stiffness of neck.....	94%
Hamstring tightness	87%
Weakness or paralysis.....	85%
Stiffness of back.....	83%

ease. Paresthesia, usually described as "numbness," occurred in four per cent of patients, but on gross sensory testing, true hypaesthesia was not observed by us. Another relatively rare symptom was hyperaesthesia (three pr cent).

The *cardinal physical signs* (Table IV) are stiffness of neck, hamstring "spasm" or tightness, weakness or paralysis and stiffness of the back. Muscle "spasm" or tightness, in which the muscle

belly becomes firmer and shortened, with increased prominence of its tendons (and early in association with pain and tenderness) may occur in any muscle group. Most frequently the posterior groups in the neck, back and legs are involved and, less commonly, the lateral muscles of the thigh, quadratus lumborum, pectoralis major, brachial biceps, sternocleidomastoids and intrinsic muscle of the hands and feet. Descriptive terms presumably due to a combination of muscle "spasm" and meningeal irritation, and frequently used in the diagnosis of poliomyelitis, are "head drop", "poker back" and "tripod position". The latter is used to described the posture which the patient assumes on attempting to sit up, with knees flexed, "poker back" and hands placed behind him for support.

Paralysis, when present, is flaccid, although in a rare patient, true spasticity, associated with pathological reflexes, may be observed. Any somatic muscle in the body may be weakened or paralyzed and the distribution of involvement is spotty. Weakness or paralysis occurs more frequently in the extremities than in the trunk and, in the former, the anterior tibialis, dorsiflexors of the foot, deltoid, triceps and opponens muscles in the hand are very commonly affected. Decreased or absent deep reflexes are associated with the flaccid paralysis, but not infrequently one may find hyperreflexia at the height of the pre-paralytic phase.

Special emphasis is placed on the *bulbar-respiratory group* of cases because it is within this group that the risk of death is greatest and accurate diagnosis of the specific type of disease is of paramount importance. In this paper the term bulbar is used broadly and includes all cranial nerves as well as medullary centers. The percentage distribution of these types of patients varies considerably from one epidemic to another. Of the 303 patients admitted to Colorado General Hospital, 96 or 32 per cent had some form of the bulbar type of disease and 55 or 18 per cent had transient or permanent respiratory paralysis. The symptoms and signs of the bulbar type of poliomyelitis depend upon the site and extent of individual cranial nuclear destruction. Lesions in the nuclei of cranial nerves III, IV and VI lead to disturbance in accommodation, diplopia, blurring of vision, ocular palsy and pupillary stasis; in the nucleus of the third division of V, to difficulty in mastication; in the nucleus of VII, to facial palsy; in the nucleus of XII, to

disturbed mastication and deviation of the tongue; in the nucleus ambiguous (IX, X and XI), to nasal speech, regurgitation of food via the nose, dysphagia, deviation of the uvula, absent gag reflex, pooling of salivary secretions, hoarseness, stridor, aphonia and the finding of vocal cord paralysis or "spasm". According to Baker et al (17 a, b), the outstanding clinical manifestations of respiratory center involvement were irregular and shallow respirations, mild to moderate tachycardia, hypertension; and the outstanding manifestations of circulatory center involvement were marked tachycardia, low pulse pressure, weak pulse and cherry-red color of the skin. Hyperthermia and marked sweating may be present.

The incidence of individual cranial nerve lesions as it occurred in 96 patients with bulbar poliomyelitis in the Colorado General Hospital series is given in Table V. Many of the patients had multiple lesions and 82 or 85 per cent, clinically, had involvement in the nucleus ambiguous (motor nerves IX, X and cranial division of the XI which are difficult to differentiate individually). Three patients had laryngeal signs and symptoms (cranial nerve X) without paralysis of soft palate or pharyngeal muscles. Two patients with paralysis of the muscles of mastication, one of whom has had residual weakness for at least two years, were particularly interesting.

Paralysis of the respiratory muscles, e.g., diaphragm and intercostals, due to lesions in the lower motor nuclei of the cervical and thoracic cord, leads to dyspnea, inability to cough and signs and symptoms of hypoxia unless artificial respiration is administered. Occasionally, one may observe decreased expansion and splinting of the chest wall apparently due to "spasm" of the intercostals and, sometimes, of the pectoralis major and latissimus dorsi. In the author's experience, hot moist packs about the chest may help relieve such symptoms and, on several occasions, appeared to forestall the use of the respirator. Whether or not "spasm" of the diaphragm occurs is speculative. Signs of paralysis of the diaphragm are an immobile, scaphoid abdomen and, excluding glottic and abdominal muscle paralysis, the inability to cough. In the event of intercostal paralysis and an intact diaphragm, on inspiration one may observe immobility or even compression of the rib cage associated with increased abdominal excursion.

Loss of abdominal muscle power may further intensify the latter symptom, as well as cause inability to cough (18).

Patients with respiratory muscle paralysis may have, in addition, involvement of any cranial nerve nucleus and/or the respiratory circulatory center, e.g., the bulbar-respiratory form. These constitute the most serious types of cases. Of considerable concern are those patients who have pharyngeal and laryngeal paralysis with dysphagia, pooling of salivary secretions in the oropharynx, aphonia and loss of the cough reflex. In the presence of respiratory paralysis the threat of aspiration, atelectasis, pneumonia and pulmonary edema is intensified whether the patient continues on his own with partially functioning respiratory muscles, or receives respiratory aid artificially. The combination of cervico-thoracic and respiratory or circulatory center lesions may exist and the chances of survival of such a patient are slim.

The outstanding clinical signs and symptoms of the encephalitic type of poliomyelitis, which occur relatively rarely and are difficult to differentiate from hypoxia, are drowsiness, anxiety, mental confusion, hyperexcitability and convulsive phenomena. As pointed out by Baker et al (17 a, b), because of the marked similarity between the manifestations of the encephalitic type of disease and hypoxia which is commonly seen in the bulbar forms, the latter should be ruled out before the diagnosis of encephalitis is made. In the Colorado General Hospital group, a relatively large number of the bulbar-respiratory patients had the above symptoms, but causes for hypoxia were known to be present. Only three patients, all children, were eventually labelled as having the encephalitic type of disease and all had associated muscular weakness. Thus in any patient with the signs and symptoms of encephalitis, it would be wise first to rule out the factors causing hypoxia, and if no associated weakness or paralysis is present, to consider seriously other types of virus encephalitides before making a final diagnosis of poliomyelitis. Unfortunately, in the latter group of cases, results of serial antibody studies are not likely to be obtained for two months or more.

Laboratory procedures, exclusive of virus studies and examination of the spinal fluid, are of little diagnostic value except in a negative sense. Total white blood cells may be normal, or elevated to 20,000 with a normal differential,

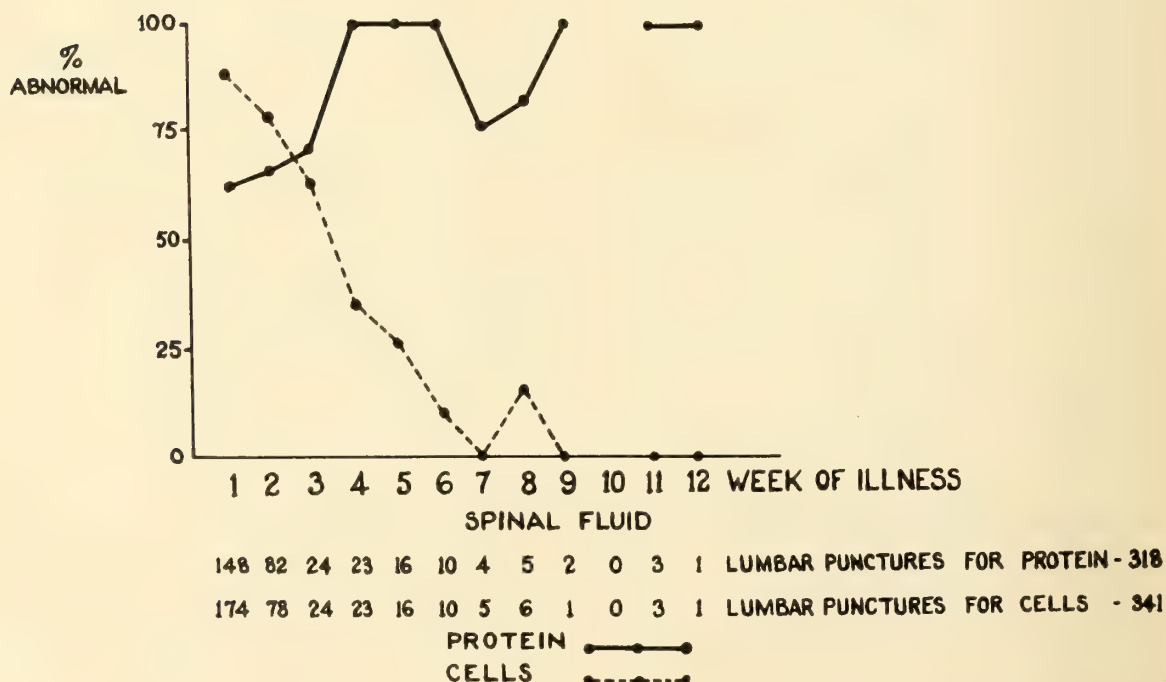
or pronounced predominance of polymorphonuclear leucocytes. Sedimentation rate is normal in uncomplicated cases. To date, a reliable skin sensitivity test has not been devised. Facilities for virus studies can be made available only for special investigation.

The spinal fluid findings, although not diagnostic, can be of considerable assistance. Changes occur in the cells and protein levels only. However, it is believed advisable to do routine cultures and sugar determinations on all patients suspected of poliomyelitis because of the ease with which this disease may be confused with early pyogenic or tuberculous meningitis. In the majority of patients the cell count is elevated during the acute phase with a decline in the early weeks of the disease. An increasing protein level reaches its maximum after this period. Fig. II shows the percentage of abnormal recordings on 283 patients who had lumbar punctures. The cell count was considered normal if it did not exceed 10 lymphocytes and if no polymorpho-

nuclear leucocytes were present ; a protein level, normal, if it was below 45 mg per cent. Note the following points: (1) the high percentage of patients with abnormal cells in the first week (88 per cent) with a rapid decline by six weeks; (2) the relatively smaller number with abnormally high levels of protein in the first week (62 per cent) with a rise to include 100 percent of all patients with spinal punctures done in the fourth, fifth and sixth weeks. In the 11th and 12th weeks of disease, in all four patients on whom determinations were done, the protein level was still elevated. However, after the fourth week, the number of determinations were relatively small. Thus, we are inclined to believe that if spinal punctures are done early in the second month of disease, abnormality of protein levels may be found. In a study by Peabody, Draper and Dochez (19) spinal fluid protein levels were found highest in the third week with a trend toward normal in the fourth week of the disease.

(Fig. 2)

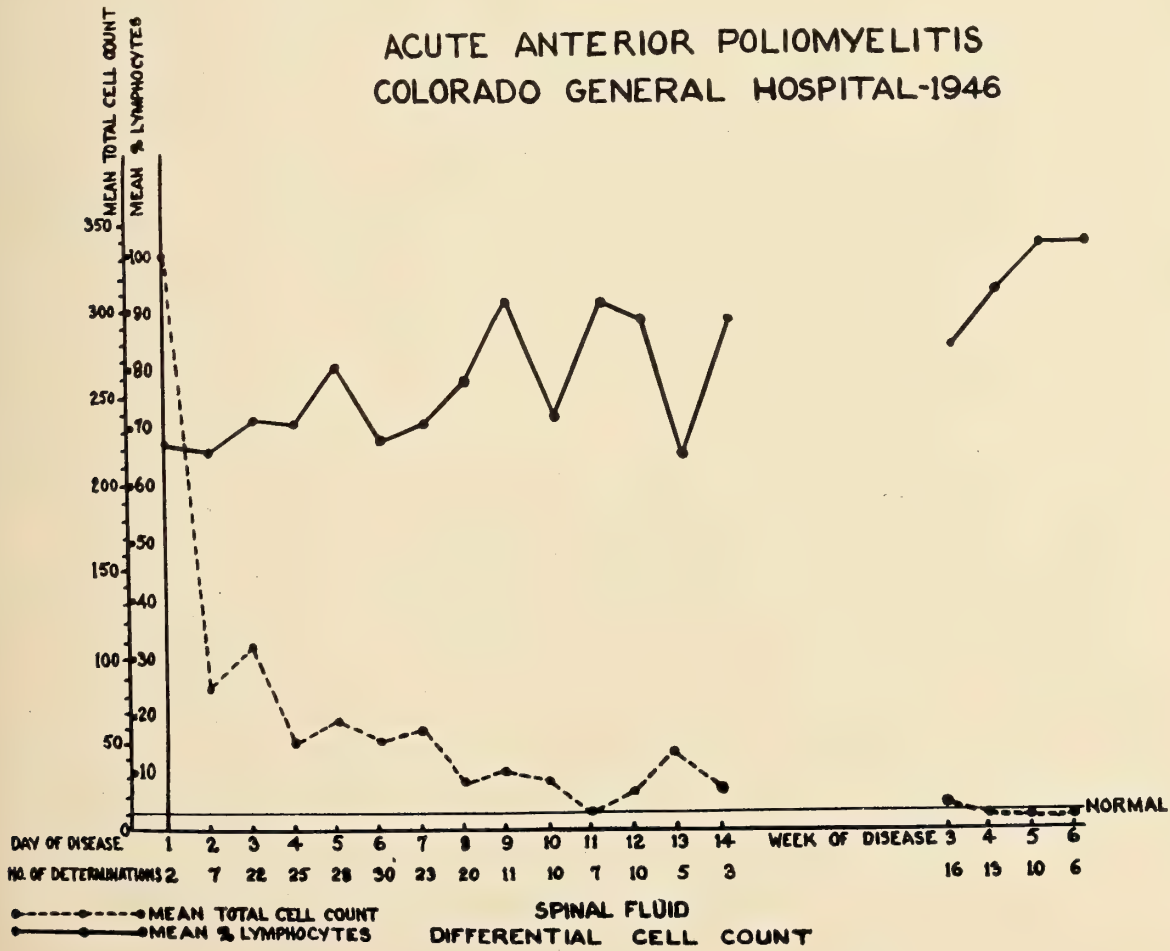
ACUTE ANTERIOR POLIOMYELITIS COLORADO GENERAL HOSPITAL-1946



As represented in Fig. III, a predominance of lymphocytes with *mean* percentage values between 63 to 100 per cent on a total of 248 determinations was found during the first six weeks of disease. Contrary to the general concept that polymorphonuclear leucocytes predominate during the first few days, mean values for lymphocytes of 66 to 71 per cent were observed in the first three days and 66 to 80 per cent in the first week of disease. Not until the period of the fifth and sixth week when normal total counts were found did the percentage of lymphocytes reach 100 per cent. When a relatively small number of cells were present, the majority of differential counts were done by the chamber method, and it should be emphasized that in differentiating granulocytes and lymphocytes by this method, errors can easily occur. However, in the first week of disease in 13 of 137 determinations and in the second week in 14 of 66 determinations, polymorphonuclear leucocytes were over 50 per cent of the total number of cells.

The peaks of the spinal fluid cell count and protein level to be expected are demonstrated in Fig. IV in which mean values on 341 determinations of the cell count and 318 determinations of the protein level are recorded. The highest cell counts occurred in the first week and highest protein levels occurred in the sixth week of the disease. However, a great range of variation in both the spinal fluid cell count and protein levels can be expected and this fact should be considered before reaching a diagnosis on any individual case. In the above series of patients, cell counts ranged from zero to 1700 per cm. and protein levels from 10 to 600 mg. per cent. A question which frequently arises is: Can a diagnosis of poliomyelitis be made in the presence of a normal spinal fluid? In our experience, such may be true during the *first three weeks* of the disease in which period the spinal puncture is most likely to be done. In the Colorado General Hospital's series of 283 patients on whom this procedure was done during this period, 21

(Fig. 3)



or seven per cent had normal spinal fluid findings. In these particular patients repeat lumbar punctures were not done after the third week of disease.

DIAGNOSTIC ERRORS

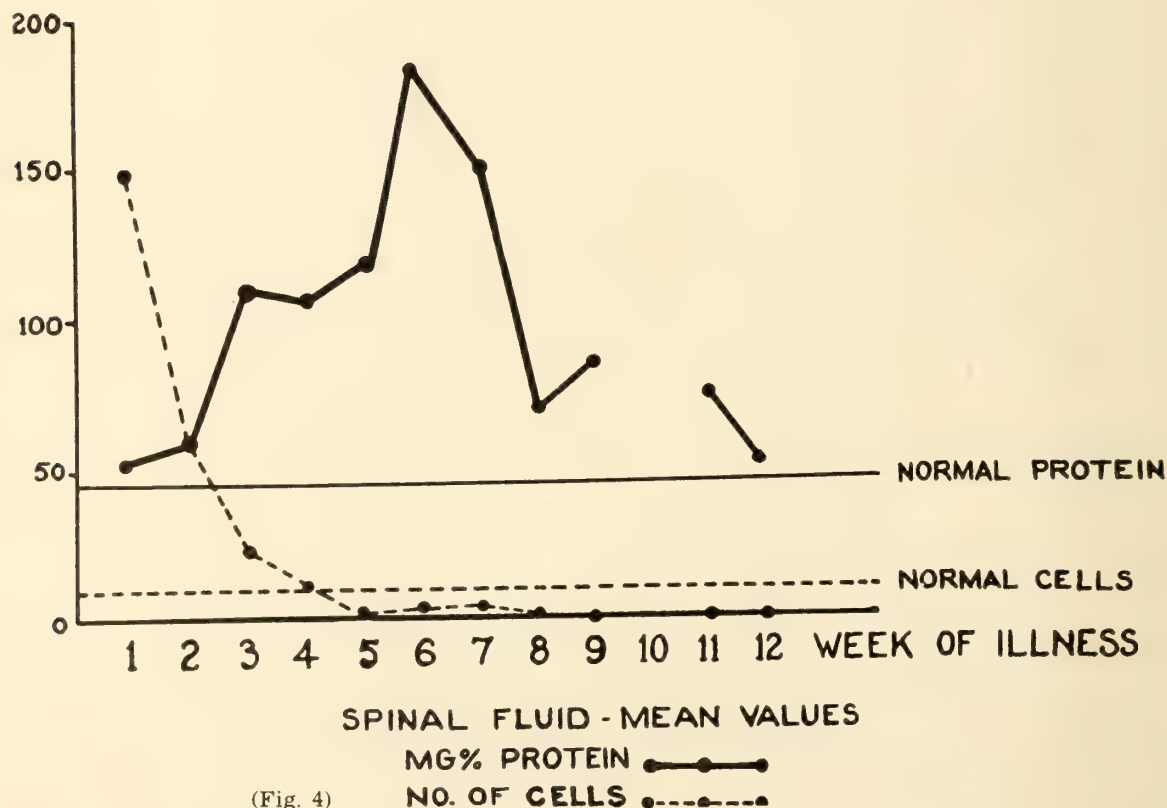
Errors in diagnosing poliomyelitis when it is not present have been unusually high, apparently due to the wide variety of forms the disease may take and, in part, to the hysteria accompanying epidemic outbreaks. At the Colorado General Hospital, of the 339 cases admitted as cases of poliomyelitis in the epidemic of 1946 (20), eight per cent proved to have other diseases and an additional four per cent could not be definitely diagnosed. On the other hand, in the non-epidemic year of 1947, 42 per cent of the cases admitted as poliomyelitis proved to have other diseases. Such figures point to the importance

of facilities for managing the "suspect" patient when setting up a poliomyelitis service. Table VI gives a listing of the various diseases with which poliomyelitis has been confused and represents the combined data from a survey of the literature, the cases admitted to the Colorado General Hospital in 1946 and 1947 (20), and the author's experience.

Again, for simplification, the various diseases are listed in Table VI under headings of the three main clinical phases of poliomyelitis, e.g., (1) *systemic*, (2) *meningitic* and (3) *paralytic*. In the systemic phase the main disease with which poliomyelitis may be confused are: acute upper respiratory infections; acute exanthematous diseases in the pre-exanthem stage; acute infectious hepatitis in the pre-icteric stage; acute infections with gastro-intestinal symptoms and

ACUTE ANTERIOR POLIOMYELITIS

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serum reactions in the non-eruptive form. In the meningitic phase, poliomyelitis may be confused with the following: (1) diseases manifesting signs and symptoms of meningeal irritation, e.g., pyogenic, tuberculous and syphilitic meningitis, lymphocytic choriomeningitis, meningismus associated with acute infections, the acute encephalitides, acute infectious mononucleosis and hepatitis and brain abscess; (2) diseases manifesting paravertebral or leg muscle tightness, e.g., acute rheumatic fever, acute osteomyelitis, acute myositis, trichiniasis, tetanus and osteoarthritis; (3) comatose states, e.g., diabetic coma, heat prostration, hypertensive encephalopathy and drug poisonings and (4) anxiety states. In the paralytic phase, the following categories of diseases have been confused with poliomyelitis: (1) diseases causing true flaccid paralysis, e.g., acute polyneuritis, transverse myelitis, spinal cord injury, hematomyelia, lead poisoning and acute encephalomyelitis; (2) diseases causing upper motor neuron paralysis, e.g., expanding central nervous system lesions, botulism, cerebral vascular accidents and embolic injury to the brain as occurs in congenital heart disease and subacute bacterial endocarditis; (3) diseases in which pseudoparalysis may be manifested, e.g., hysteria, acute rheumatic fever, osteomyelitis, acute myositis, acute epiphysitis, septic arthritis, rickets and scurvy and (4) mild cyanide poisoning in which symptoms of hypoxia due to lowered tissue oxygenation simulates a respiratory paralysis.

APPRAISAL OF THE PATIENT

From the foregoing comments on the incidence

of the wide range of diagnostic errors and variations in the clinical picture and course of this disease, the following facts become apparent:

(1) With inclusion of "abortive" cases, poliomyelitis is a relatively common disease and one which can affect any age group.

(2) All pertinent clinical data should be carefully weighed before making a definite diagnosis of poliomyelitis.

(3) With the established diagnosis of poliomyelitis including a definition of type, it is desirable to attempt to evaluate the patient from the standpoint of management and future prognosis.

In reference to (1) poliomyelitis should be included in the differential diagnosis on any patient exhibiting signs and symptoms of an acute infectious process or neuromuscular disorder of acute onset, particularly during the warm months of the year. In a high percentage of cases of frank poliomyelitis, a reasonably definite diagnosis can easily be made on the grounds of fever, headache, meningeal signs, muscle tightness, flaccid paralysis and/or spinal fluid changes as outlined above. However, in many patients, the diagnosis must be made on an exclusion basis and evaluation of individual symptoms becomes important. In our experience, diarrhea has occurred rarely and when present, was believed most likely due to a concomitant enteric infection. Other workers have found this symptom common in some epidemics. (21) The observation that 11 per cent of our patients complained of abdominal pain which was often associated with vomiting, abdominal muscle spasm and

TABLE V
POLIOMYELITIS, COLORADO GENERAL HOSPITAL, 1946

Cranial Nerve Involvement with One or More Corresponding Symptoms	
Total Number of Bulbars.....	96
Cranial Nerves IX, X and XI (Cranial Division).....	82
(nasal speech, regurgitation of food via nose, dysphagia, pooling of secretions, hoarseness, aphonia, stridor)	
Cranial Nerve X (Singly).....	3
(hoarseness, aphonia, stridor)	
Cranial Nerve VII	21
(facial palsy)	
Extra Ocular Nerves (III, IV, VI).....	10
(diplopia, blurring, disturbance in accommodation)	
Cranial Nerve XII	9
(difficulty in mastication and speech)	
Cranial Nerve V (3d Division).....	2
(difficulty in mastication)	

tenderness explains the occasional case which can be erroneously diagnosed as acute appendicitis. Symptoms of a "cold" are often cited as an early manifestation of poliomyelitis. However, in the author's experience, on careful questioning of the patient, actual coryza occurs rarely and probably no more frequently than late summer allergic rhinitis and the common cold among the general populace. On the other hand, hoarseness or dysphonia, although of relatively rare incidence in a cross section of poliomyelitis cases, should not be taken lightly in a patient suspected of having poliomyelitis, for this symptom may be the first manifestation of glottic muscle paralysis and be proven only by visualization of the cords. Shaking chills or chilliness, common manifestations of acute infections, are relatively infrequent in this disease and, if prominent, poliomyelitis is unlikely or complicated by a pyogenic infection. On routine history-taking, the patient will occasionally state that he had "numbness" in an extremity, but in the author's experience, "numbness" to the patient with poliomyelitis has almost invariably meant loss of power associated with a sensation of heaviness, and on gross sensory testing, definite hypaesthesia or loss of vibratory sense could not be demonstrated. More credence, however, is given to the existence of hyperaesthesia, because in such patients light stroking of the skin or weighty bed clothes often evokes discomfort. This symptom has been observed to occur more commonly during the pre-paralytic phase. Because of the rarity of convulsions unassociated with hypoxia in poliomyelitis, pyogenic meningitis or a virus encephalitis should be first considered in a patient exhibiting this symptom, together with fever, meningeal signs and mental aberrations.

Occasionally one sees a patient exhibiting a mild degree of real spasticity associated with a positive Babinski. With the observation that in fatal cases the motor cortex of the precentral gyrus is almost uniformly, although mildly, involved, clinical signs of upper motor neuron lesions could be expected in some cases. In the author's experiences, these patients respond poorly to hot packs or hydrotherapy and easily develop contractural deformities. Such was true in two of the three children who were diagnosed as encephalospinal type of disease.

The most careful attention in making a definite diagnosis as to type of disease should be given to the bulbar-respiratory group of patients

because life itself is threatened. As mentioned previously, the manifestations of hypoxia are frequently superimposed on the pre-existing disease picture and the physician needs first to recognize the signs and symptoms as due to hypoxia and, secondly, to determine the basic etiology in order to institute the proper therapeutic approach. The symptoms of lowered oxygenation or hypoxia as related by Baker et al (16 a, b) are first restlessness, apprehension, anxiety and rising pulse, all of which can become manifest before the appearance of cyanosis. If hypoxia is unrelieved or allowed to increase; dyspnea, cyanosis, mental confusion, convulsive phenomena, delirium, coma and death will ensue. The basic causative factors of hypoxia in a patient with lesions in the nucleus ambiguus is obstruction of the airway, either by salivary secretions and food, or vocal cord paralysis; in the respiratory center, deficient or inefficient control of respirations; in the circulatory center, vascular collapse, impaired cardiac filling and output; and in the cervico-thoracic cord, impaired respiratory muscle function. Pulmonary edema is an end result of any of the above conditions and is further intensified by the existent hypoxia.

Admittedly it is extremely difficult to prognosticate the immediate outcome for any individual patient during the acute phase of the disease, but a careful evaluation of certain clinical criteria can be helpful in immediate management and expectant treatment. In general, development or increase of paralysis is unlikely after fever and signs of toxicity have subsided. Local muscle tenderness or hyperaesthesia in the febrile stage oftentimes heralds weakness or paralysis of underlying muscle groups and, similarly, painful respirations with splinting of the chest may be a precursor to respiratory paralysis. Weakness or paralysis of an upper extremity should alert one to the possibility of ensuing involvement of the diaphragm and intercostal muscles. As mentioned above, a patient with a history and signs of a sore throat is more likely to develop the bulbar type of disease. A patient with ophthalmoplegia or facial palsy is a likely candidate for more serious symptoms such as pharyngeal, laryngeal or respiratory-circulatory center paralyzes.

Although patients can be expected to have some continued return of muscle function up to 18 months or two years, near maximum return seems to occur usually during the first six months

TABLE VI POLIOMYELITIS

Diagnostic Errors

I. SYSTEMIC PHASE

Acute upper respiratory infections
Acute exanthematus diseases, e.g.,
 scarlet fever, rubella, rubeola
Acute infectious mononucleosis
Acute infectious hepatitis
Acute gastroenteritis
Acute appendicitis
Pneumococcus peritonitis
Septicemia

II. MENINGITIC PHASE

Pyogenic meningitis
Tuberculous meningitis
Syphilitic meningitis
Lymphocytic choreo-meningitis
Meningismus with acute infections
Acute infectious mononucleosis
Acute infectious hepatitis
Acute rheumatic fever
Brain abscess
Acute osteomyelitis
Acute myositis
Trichiniasis
Tetanus
Osteoarthritis
Diabetic coma
Heat prostration
Hypertensive encephalopathy
Drug poisonings

III. PARALYTIC PHASE

Acute polyneuritis
Spinal cord injury
Hematomyelia
Lead poisoning
Acute encephalomyelitis
Expanding c.n.s. lesions
Botulism
Cerebral vascular accident
Congenital heart disease
Subacute bacterial endocarditis
Hysteria
Acute rheumatic fever
Osteomyelitis
Acute myositis
Acute epiphysitis
Aseptic arthritis
Rickets
Scurvy
Cyanide poisoning

and perhaps even during the first three months after onset of the disease. In those muscle groups in which complete loss of motor function occurs and absent deep reflexes are found, an eventual return to functional power is unlikely.

The severity of disease in individual epidemics may vary considerably. In the Colorado General Hospital group of patients, with periods of hospitalization varying from eight days to one year (data compiled in September 1947), the degree of involvement on discharge was as follows: No residual, 24 per cent; minimally disabled (minimal impairment in function and no aids required), 31 per cent; moderately disabled (non-function of one extremity requiring support and/or aids in ambulation), 24 per cent; severely disabled (non-function of two or more extremities requiring support and/or aids in ambulation), nine per cent, completely disabled (bed-ridden), two per cent; deaths, eight per cent; hospital transfers (children early in epidemic), two per cent. However, as mentioned previously, this group of patients is probably heavily weighted with bulbar and severely paralytic types. Figures on the outcome of another epidemic are those from Maryland, 1941 (5), in which in a total of 296 patients, 50 per cent had no after-effects; 29 per cent slight after-effects ("practically normal movements"); 18 per cent marked after-effects and the mortality rate was three per cent.

Summary

1. The diagnosis of poliomyelitis is discussed and supported by presentation of the clinical data on 303 patients admitted to the Colorado General Hospital during the epidemic of 1946.

2. The clinical course of this disease is presented by description of the systemic, meningitic and paralytic phases with a classification of disease types based on the period at which the process becomes arrested.

3. The most common symptoms of frank poliomyelitis were fever, headache, anorexia, nausea, vomiting, pain in neck, back and legs, constipation, drowsiness and malaise; diarrhea, cough, coryza, chills and convulsions occurred rarely; sore throat is believed to be an important symptom in heralding the bulbar type of disease. In a group of 96 bulbar cases, cranial nerves IX, X and cranial division of XI were most frequently involved.

4. Cardinal physical signs were stiffness of the neck and back, hamstring tightness and muscular weakness or paralysis.

5. Spinal fluid cell counts were highest in the first week and can be expected to return to normal by the end of the fourth week. The protein level may be only slightly elevated during the first three weeks and reach its maximum in the fourth, fifth and sixth weeks of the disease. Negative spinal fluid findings during the first three weeks of the disease do not rule out a diagnosis of poliomyelitis.

6. The variety of diseases with which poliomyelitis can be confused is great, and the high incidence of diagnostic errors indicates a real need for provision of a screening admission clinic where an initial physical examination and spinal puncture may be done, and of observation rooms for the "suspect" cases.

7. A careful appraisal of the patient is important from the standpoint of diagnosis, classification of type of poliomyelitis in respect to the bulbar and respiratory group and immediate management of the patient.

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DIETHYLSTILBESTROL (DES) IN TREATMENT OF THREATENED ABORTION

By

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In 1941 the author (1) demonstrated empirically the value of estrogen therapy in treatment of threatened and habitual abortion and of premature labor. Five years later, this high-estrogen therapy was put on rational basis by Smith, Smith and Hurwitz (2) at Boston Lying-In Hospital. The author's former publications have shown that, contrary to previous fears concerning the effects of estrogens during pregnancy, the tolerance for diethylstilbestrol by the pregnant woman is at least a thousand times that of the non-pregnant woman.

Reported herewith are 21 unselected patients with threatening abortion treated with varying

amounts of diethylstilbestrol. Although dosage varies with each individual, the required amount being that which stops cramps, spotting, bleeding and pain, the following dosage regimen may generally be employed:

In the milder cases, patients with spotting and mild cramping for 4 to 12 hours, 100 milligrams are given every 15 minutes until cramps, pain and spotting stop. Then 25 milligrams three times a day are given for one week.

A dose of 25 milligrams is then given each morning up to the 8th month of pregnancy. If pain cramps and bleeding recur, doses of 100 milligrams are administered every 15 minutes until these symptoms are dispelled. Then 25 milligrams 3 times a day and once at night are given for 2 weeks, then 50 milligrams every

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morning for 2 weeks and then 25 milligrams every morning thereafter until the 8th month. All single daily dosages are given in the morning when they are most effective in allaying uterine contraction caused by usual daily activity.

In moderately severe cases of threatened abortion, patients with cramps, spotting and bleeding for 12 to 24 hours, 250 to 500 milligrams in oil or aqueous suspension are injected into the gluteal muscles through a long spinal needle. The needle is inserted downward toward the gluteal fold making the solution less apt to be lost. Doses of 200 milligrams are given orally every 15 minutes until all signs and symptoms are controlled. Tablets of 25 milligrams, or its equivalent liquid preparation, are given 3 times daily and at bed time for 2 weeks, and every 3 to 7 days doses of 250 to 500 milligrams in aqueous suspension are given intramuscularly. After 2 weeks of this treatment, the patient is given 25 milligrams 3 times daily for two weeks, then 25 milligrams twice daily for one week and 25 milligrams daily thereafter until the 8th month. If cramps, spotting, pain or bleeding recur, an emergency dose of 50 to 100 milligrams is given orally, either as tablets or liquid.

In severe type of threatened abortion, with cramping, bleeding and pain for 2 to 4 days, doses of 250 to 500 milligrams in aqueous suspensions are given into the buttocks. Concurrently 250 milligrams to 1000 milligrams are given by mouth, tablets or liquid, every 15 minutes until symptoms are relieved. When this occurs, 250 to 500 milligrams are given intramuscularly every third day for 2 to 4 weeks. For 2 weeks, 100 milligrams are given 3 times daily at bed time. Doses of 25 milligrams are then given 3 times daily and at bed time, for two weeks, 25 mg., four times daily for 2 months, then one, 25 mg. tablet daily until the 8th month.

Careful and complete physical examination of each patient is made and appropriate diets with special attention to vitamins are prescribed. One hundred and twenty-five consecutive patients with threatened abortion over the past nine years were given diethylstilbestrol. Not any of these patients were given bed rest which is now believed to be unnecessary. Bed rest is also good treatment but if stilbestrol is given bed rest is not needed except in a very few cases. Most know that a patient rather be up and about and take tablets than to have to stay in bed. Yet if go-

ing to bed stops cramps, pains and vaginal bleeding then the patient is kept in bed for 4 to 7 days. The following laboratory determinations were made at approximately monthly intervals: red and white blood cell counts, hemoglobin, sedimentation rate, coagulation time, bleeding time, blood serum cholesterol, blood chlorides, blood uric acid, fasting blood glucose, specific gravity of urine, urinary albumin and urinary sugar. Only abnormal laboratory findings are reported.

Illustrative of these 125 cases of threatened abortion the following 21 cases are reported in detail:

Case 1. R.A.A. White. Age 31. First pregnancy: female, now 9 years old and well. Second pregnancy: male, term, now 6 years old and well. Third pregnancy: day 63 stilbestrol therapy begun, weekly intramuscular injections. Day 120 abortion threatened with cramps for 3 days. Day 131 pain in lower abdomen. Day 154 pain in both sides. Day 170 severe backache. Day 200 backache recurred and persisted for 1 month. Day 253 abortion threatened with severe pain and cramps in lower abdomen. Day 260 but little pain in lower abdomen. Day 281 delivered of normal female. Total stilbestrol dosage 120,655 milligrams in 125 days. Laboratory: hemoglobin fell from 86 to 70 during 8th month.

Case 2. D.L.M. White. Age 26. First pregnancy: miscarried at 6month, cause coitus. Second pregnancy: day 205 pain in abdomen, stilbestrol started. Day 299 severe abdominal cramps continuing intermittently until delivery, worse on days 231 and 258. Day 258 severe cramping and contraction. Day 268 delivered of normal female. Total stilbestrol dosage 45,500 milligrams in 63 days. Laboratory: slight fall in hemoglobin toward end of pregnancy.

Case 3. J.A.R. White. Age 20. First pregnancy: bleeding at approximately weekly intervals for one hour, cramps and pain in leg. Day 25 stilbestrol begun. Day 161 pulling sensation in both lower abdominal quadrants following a fall. Day 163 fainted and fell, bleeding, which was controlled by additional stilbestrol. Day 215 cramps lasting about a week controlled by intramuscular stilbestrol. Day 253 stilbestrol stopped. Day 270 delivered of normal female. Total stilbestrol dosage 7,410 milligrams in 229 days. Laboratory: negative.

- Case 4. F.S. White. History of old endometriosis. First pregnancy: day 74 stilbestrol started and continued until day 104. Day 138 stilbestrol resumed because of plain low in abdomen especially after riding. Day 225 hard contracting uterus, stilbestrol to control cramps. Day 249 stilbestrol stopped. Day 263 delivered normal female. Blood loss 175 cc. Total stilbestrol dosage 27,850 milligrams in 141 days. Laboratory: increase in hemoglobin and leukocytes just before delivery.
- Case 5. N.H.W. White. First pregnancy: term. Second pregnancy: day 77 abortion threatened with gush of blood, stilbestrol for 6 days. Day 190 painless bleeding, 250 milligrams stilbestrol daily. Day 240 stilbestrol stopped, Caesarian section following several days of bleeding. Total stilbestrol dosage 1,680 in 56 days. Laboratory: fall in hemoglobin. Urinary albumin and sugar in 8th month.
- Case 6. G.P.W. White. First pregnancy: Day 37 stilbestrol started and continued until day 57. Day 89 bleeding and severe backaches for two weeks, stilbestrol resumed. Day 113 cramps. Day 148 stilbestrol stopped. Day 276 delivered of normal male. Total stilbestrol dosage 2,620 milligrams in 81 days. Laboratory: negative.
- Case 7. M.S.S. White. Age 24. History of sterility. Stilbestrol 0.5 milligram daily to produce ovulation. First pregnancy: during last menstrual cycle spotted on day 21, flooded on day 22 and spotted on day 23. On day 45 of menstrual cycle (day 31 of pregnancy) backache and cramping in lower abdomen but not bleeding, stilbestrol started. Day 62 severe backache. Day 155 cramping controlled by additional stilbestrol. Day 206 cramping controlled by additional stilbestrol and continued until delivery. Day 297 delivered normal male. Total stilbestrol dosage 30,000 milligrams in 266 days. Laboratory: reduced leukocytes just before term. Trace of urinary albumin in 8th month.
- Case 8. A.H.N. White. Age 23. First pregnancy: Day 63, 15 milligrams stilbestrol as test for pregnancy. Day 68 daily doses of stilbestrol started. Day 98 spotting without cramps. Day 99 aborted. She had been examined that day and small amount of blood in vagina, and about 6 hours later passed fragment of placenta. Total stilbestrol 86,215 milligrams in 33 days. Laboratory: negative.
- Case 9. L.M.P. White. Age 33. History of endometriosis treated with stilbestrol. First pregnancy: Stilbestrol 0.5 milligram started. Day 27 abortion threatened with bleeding for two days. Day 29 stilbestrol 25 milligram tablets started because of bleeding. Day 76 and 80, abortion threatened with bleeding, but controlled by additional stilbestrol. Stilbestrol continued until delivery. Day 257 delivered normal female. Total stilbestrol dosage 16,728.5 milligrams in 235 days. Laboratory: negative.
- Case 10. V.K. White. Age 36. First pregnancy: starting on day 21 abortion threatened with cramping and pain in lower abdomen continuing for 3 weeks. Day 51 stilbestrol started and continued to delivery. Day 145 abortion threatened with cramping controlled by additional stilbestrol. Intermittent cramping until day 200. Day 270 delivered of normal female, easy delivery with 200 cc. blood loss. Total stilbestrol 43,475 milligrams in 228 days. Laboratory: negative.
- Case 11. J.P.K. White. Age 20. First pregnancy: Day 67 flood. Day 68 stilbestrol started and continued until aborted on day 131. Cramping moderate to severe, backache, spotting and bleeding all through pregnancy but controlled with large doses of stilbestrol. Day 129, 1000 milligrams intramuscularly. That afternoon membranes ruptured and there was severe pain. Day 131 aborted. Total stilbestrol 32,425 milligrams in 63 days. Laboratory: negative.
- Case 12. L.W.P. White. Age 29. First pregnancy: day 24 abortion threatened with cramping and pressure in vagina lasting 6 days, stilbestrol started. Day 38 stopped medication on own accord—did not want to take pills because of nausea and has to eat too much to control nausea. Day 45 aborted, blighted, profuse hemorrhage for 11 days before abortion. Total stilbestrol dosage 66.25 milligrams in 15 days. Laboratory: trace of urinary albumin 2 weeks after abortion.
- Case 13. M.O.K. White. Age 17. First pregnancy: Day 59 stilbestrol started and continued until day 75 when abortion occurred, normal fetus, excess decidual reactions, grossly. Total stilbestrol 1200 milligrams in 12 days. Laboratory: Frog test positive on day 54.

Cast 14. G.H. Colored. Age 18. First pregnancy: term, male, now 10 months old and well. Second pregnancy: first examination February 7, 1949 showed uterus size of 4 months pregnancy. Menstrual history dated periods December 24, 1948, and January 26, 1949, normal periods. February 7, 1949, stilbestrol started. Large doses of stilbestrol were given by mouth and by intramuscular injection until delivery of normal female May 17, 1949. Total stilbestrol dosage 192,100 milligrams in 99 days. Laboratory: low hemoglobin throughout pregnancy.

Case 15 S.P.F. White. Age 23. First pregnancy: Two year old child living and well. Second pregnancy: aborted at 6 month, two years before present pregnancy. Third pregnancy: day 137 threatened to abort with bloody discharge, heavy bearing down sensation and sharp abdominal pains. Day 139 stilbestrol given. Day 149 routine stilbestrol started and continued at intervals when cramps occurred to time of delivery. Total stilbestrol dosage 3,950 milligrams in 18 days. Laboratory: hemoglobin low throughout pregnancy. Albumin and faint trace of sugar in urin at time of delivery.

Case 16. W.R.B. White. Age 25. First pregnancy: Day 54 stilbestrol started. Day 128 abortion threatened with bleeding for 3 days. Day 266 delivered of normal female. Total stilbestrol dosage 20,625 milligrams in 163 days. Laboratory: negative.

Case 17. A.J.G. White. Age 27. First pregnancy: male, now 17 months old, weight 7 pounds, 11 ounces at birth. Second pregnancy: Day 106 stilbestrol started. Day 161 slight cramping. Day 203 occasional cramps. Day 213 cramps of abortion controlled by 650 milligrams stilbestrol. Day 220 delivered of normal male. Laboratory: low white blood cell count just before and one month after delivery.

Case 18. L.P. White. Age 33. First pregnancy: Day 29 stilbestrol started and continued until delivery. No threatening. Day 270 delivered of normal female now 3 years old and well. Total stilbestrol dosage 35,775 milligrams in 169 days. Laboratory: negative. Second pregnancy: day 33 abortion threatened with spotting and cramping, stilbestrol started. Spotting with cramps continued until day 55. Day 75 last visit to this clinic, no more stilbestrol.

Day 133 aborted. Total stilbestrol 25,937.6 milligrams in 43 days. Laboratory: negative.

Case 19. D.E.J. White. Age 31. First pregnancy: male, now age 13 and well. Second pregnancy: female, now age 9 and well. Third pregnancy: male, now age 5 and well. Fourth pregnancy: threatened to miscarry all through pregnancy, had to remain in bed entire 9 months. Delivered of female, now age 4 and well. Fifth pregnancy: days 5 and 6 abortion threatened with cramping and pain in abdomen, stilbestrol started in large doses on day 6. Cramps in abdomen continued intermittently during entire pregnancy but there was no bleeding except on days 16 and 17. Day 281 delivered of normal male, rapid delivery, 300 cc. blood loss. Total stilbestrol dosage 259,903 milligrams in 172 days. Laboratory: slight trace of urinary albumin in 8th month.

Case 20. S.G. Mexican. Age 27. First pregnancy: term, large female now age 6 and well. Second pregnancy: Day 191 stilbestrol started. Day 226 abortion threatened with cramps in lower abdomen and continued intermittently until delivery. Day 250 delivered of normal twins, boy and girl. Total stilbestrol 12,100 milligrams in 59 days. Laboratory: red cell count and hemoglobin low throughout pregnancy. Low leukocyte count toward end of pregnancy. Trace of urinary albumin in 7th month.

Case 21. B.P.C. White. Age 28. First pregnancy: Day 251 abortion threatened with cramping, pains in lower abdomen and lower back and continued until delivery. Day 256 stilbestrol started and continued until delivery. Day 288 delivered of normal male, 8 pounds, three ounces. Total stilbestrol dosage 1,600 milligrams in 32 days. Laboratory: trace of urinary sugar on day 262 and 15 days following delivery.

COMMENTS

Case 1 illustrates the advantage of stilbestrol therapy as a prophylactic against abortion. This patient was given diethylstilbestrol on day 63 preventing any threat of abortion until day 120 when increased diethylstilbestrol dosage controlled the symptoms, carrying the pregnancy to term.

Case 18 is a convincing illustration of the prophylactic value of diethylstilbestrol therapy. This patient was given diethylstilbestrol from the 29th

day of her first pregnancy until day of delivery and showed no signs of threatening abortion. In her second pregnancy abortion threatened on day 33 and was controlled by the immediate institution of diethylstilbestrol therapy. This carried the pregnancy safely until the 75th day when the patient received other medical care which did not include this therapy. She aborted on day 133.

Cases 4 and 9 illustrate the value of diethylstilbestrol in endometriosis. This therapy is discussed elsewhere.

The early prophylactic use of diethylstilbestrol is strongly recommended in all primiparae since there has been no previous opportunity of determining their proneness to abort.

There has been demonstrated repeatedly that this therapy is without harm even in the patient who would not abort even without the treatment.

Summary

1. Effective diethylstilbestrol dosage routines in mild, moderately severe and severe types of threatened abortion are outlined.

2. Massive diethylstilbestrol in 21 cases of

21 cases of threatened abortion gave fetal salvage of 76%.

3. Evidence is presented of the efficacy and harmlessness, even in primiparae, of routine massive diethylstilbestrol therapy as prophylaxis against the usual symptoms of threatened abortion.

4. Every case requires a different dose to save their threatened abortion. The amount that keeps patient from aborting is the right dose whether it be 25 mg. daily or 2500 mg. daily. Can give too little but not too much diethylstilbestrol.

5. Massive doses of diethylstilbestrol produces no damage to mother and/or child.

6. Stilbestrol will allow patient to be up and about, doing her normal duties, so eliminating short or long periods of bed rest.

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- Diethylstilbestrol products used in this study were:
- (1) Bio-des for intramuscular injection.
 - (2) des tablets
 - (3) des liquid for oral use.
- Grant Chemical Company, Inc., New York City.
329 Medical Bldg., Houston 2, Texas.

REGURGITATION ESOPHAGITIS

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Recently the authors studied a case in which regurgitation esophagitis with ulceration in the lower esophagus was an important feature. Eventually the case required surgical intervention because of stenosis of the lower esophagus. In the preoperative discussions between the medical and surgical services, the problem imposed by the irritative regurgitation of gastric contents was realized to be important in planning the surgical and postoperative management of this case. This resulted in the realization that the

subject of regurgitation esophagitis was worthy of more consideration by the medical profession. In a 1936 issue of the *A.M.A.*, Vinson and Butt (2) claimed that esophagitis occurred oftener than any other lesion of the esophagus. In their series of 3000 necropsies, 7% or 213 had esophagitis. Regurgitation of gastric juices is probably the commonest cause. Surprisingly, retrograde studies showed that only 10% of the charts of these cases contained notations pertaining to symptoms referable to the lower esophagus. In a 1943 issues of *Radiology*, L. W. Paul (5) comments in a similar manner. In contrast to the frequency of esophagitis with paradoxically few references to it the literature, there are numer-

*Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

ous articles concerning cardiospasm, congenital anomalies, strictures, diverticula, varices and tumors of the esophagus as well as functional dyspepsia, Plummer-Vinson Syndrome, perforations and foreign bodies.

The case is as follows: The history goes back to 1946 when as a 32-year old white male, he noted substernal fullness when eating. In 1947 surgery was resorted to through a thoracic approach at an Army General Hospital. The esophagus was found to be normal. A small hiatus hernia containing a chronic peptic ulcer was found and excised. A gastro-esophageal anastomosis was made. The cardia of the stomach was brought up into the thorax (to reduce tension on the suture line). The intrathoracic stomach was anchored by sutures to the paravertebral structures. The early postoperative course was stormy and complicated by left pleural effusion. Eventually, periodic dilation of the anastomotic area was instituted. In April 1949, or two years later, a few days after one such dilatation with a No. 52 Bougie, an attack of severe hematemesis occurred. The patient was hospitalized. Ten days later, barium swallow and x-ray plates showed one inch of high grade stenosis just above the gastroesophageal junction. At esophagoscopy, a marked stenosis in this general area with only a peripheral slit-like passage-way was seen. The upper surface of this stenotic shelf was occupied largely by a shallow ulcer crater. Gastric analysis revealed moderate acid values. The existing condition was believed to contraindicate more dilatation because of the trauma and hemorrhage it would involve. Instead, a strict Sippy regime was considered and instituted. Nevertheless, low sternal burning at night continued until the patient was instructed to sleep in a semi-recumbent position. This position decreases regurgitation up into the esophagus. Subsequent esophagoscopy showed the ulcer to have healed, but the shelf-like encroachment of the esophageal lumen remained. The patient was eventually allowed to leave the hospital with instructions to follow a modified Sippy regime. However, the patient cooperated only partly. Some moderate obstruction to soft food continued in the low substernal area. In November 1949, he had another severe hematemesis. Esophagoscopy again revealed the lower esophageal shelf-like obstruction but no ulcer. Instead, there was a diffuse hyperemic esophagitis in the lower esophagus. This area bled

freely at esophagoscopy without direct trauma. The Sippy regime again was made more thorough and the patient repeated his previous improvement except that the substernal obstruction now became progressively more prominent. To determine the degree of the stenosis, at esophagoscopy, bougie passage was tried cautiously. A No. 10 bougie could be passed but not a No. 12. Effective dilatation was not believed to be feasible. He was operated on in late January 1950 while the procedure was still an elective one. The left thoracic approach was again chosen. Because of diffuse adhesions, about four hours of blunt and sharp dissection was necessary to reach the gastro-esophageal area. Adjacent to and pressing on the esophagus the adhesions were particularly dense. There were severed. The esophagus was opened immediately above the anastomosis and, surprisingly, only a mild thickening of the wall was present. The mucosal surface was normal. Apparently, the recent esophagitis had cleared up on the medical program, and the shelf-like obstruction had been produced by the effects of extrinsic dense adhesions. The anterior vagus nerve was still intact and a segment of this was removed. The posterior vagus had been interrupted in 1947. A simple cardioplasty was also done. The status of the partial thoracic stomach was allowed to continue unchanged. The postoperative course was satisfactory and the patient became free of the low sternal obstruction. He was again discharged. To date he has been asymptomatic. X-rays during convalescence reveal no hindrance to the passage of barium in the lower esophagus.

ETIOLOGY:

In the March 1948 issues of C.G.O.G., Olsen reviews the literature concerning esophagitis and stated that regurgitation of gastric juice was the commonest cause. In this paper, esophageal ulcers and regurgitation esophagitis will be used interchangeably as usually the difference is only quantitative. The esophageal mucosa is generally conceded to be less resistant to peptic digestion by gastric juices than is gastric mucosa. While the esophageal mucosa contains mucous forming glands, the relative efficiency of this defense mechanism in comparison to that of the gastric mucin in the stomach is unknown. The literature claims periodically that the lower esophagus is the third most common location of peptic ulcer.

DIFFICULTIES IN THE DIAGNOSIS OF ESOPHAGITIS:

One difficulty is that many cases of esophagitis are not accompanied by manifestations that attract attention. This was the experience of P. Vinson. (2) As would be expected, the esophagoscopists wrote most of the articles concerning living patients with proven cases of esophagitis with or without ulcers or of scars in the esophagus presumed to be residuals of ulcers. Another difficulty is that the commonest symptom in esophageal ulcer or regurgitation esophagitis is discomfort that usually is called "heartburn." This is so commonly a functional complaint and treated casually by household medications that one's suspicion index is low when a case with an organic basis is encountered. If, instead of the misleading term "heartburn," a more proper designation had been popularized, peptic esophagitis with or without ulceration would be considered oftener. Also demonstration of niches by x-ray in cases of ulcers of the esophagus is the exception rather than the rule. Esophageal ulcers are usually shallow. Also peptic esophagitis may not be associated with crater formation but instead be a diffuse superficial process. Likewise, x-ray demonstration of a lower esophageal spasm is not pathognomonic of peptic pathology. Gastric ulcers, duodenal ulcers, gallbladder disease, gastritis, or psychic factors may cause reflex spasm in the area of the cardiac sphincter. Esophagoscopy by the better known rigid, open end type of esophagoscope is dangerous enough that this procedure is not a widely utilized diagnostic procedure. The new Schindler optic esophagoscope or the Boros flexible esophagoscope are very safe but are not as yet widely used. The flexible gastroscope has not helped in this field as it does not visualize the esophageal lumen since the mucosa is too close to the objective window. The lower esophagus commonly is not carefully examined at post-mortem studies. Accordingly, the frequency of peptic esophagitis is easily overlooked and its importance not fully appreciated. Regurgitation esophagitis is usually situated low but may be higher in the esophagus especially when diverticula or other hindrances exist to trap gastric regurgitation. Regurgitation esophagitis is more common when chronically lax diaphragmatic and cardiac sphincter action exists. Hiatus hernia and intrathoracic stomach are good examples of decreased

phincter action. Hiatus hernia is common after the age of 50 in obese individuals. The literature periodically describes insidious bleeding resulting from the esophagitis or peptic ulcerations co-existing with hiatus hernia. The anemia can be marked but the process obscure enough that the cause may be overlooked without adequate study. Likewise common is the more transient gastric regurgitation in narcosis, anesthesia, alcohol excess, barbiturate coma, toxic states, etc. Debilitating disease also predisposes as those conditions are usually associated with the patient spending much time in a horizontal position which favors regurgitation.

Another cause of regurgitation esophagitis is frequent belching. If, because of esthetics, the belching or burp is suppressed, more complete gastric regurgitation may occur. Regurgitation esophagitis from frequent vomiting is easily understood. A frequent cough can act similarly. In some individuals, more overloading of the stomach results in regurgitation. Some rheumatics experience low esophageal burning while on salicylate therapy. Whether in-dwelling stomach, duodenal or Miller-Abbott tubes cause or merely aggravate regurgitation esophagitis is still controversial. Relaxed tissues in senility can be a factor. In the Vinson and Butt (2) series of 213 cases of esophagitis, 75% had had major surgery shortly before. Most commonly the surgery had been done for the gallbladder, duodenal ulcer, various obstructions of the gastrointestinal tract or hiatus hernia. In 1936, Hans Selye (7) noted esophageal ulcers in experimental animals after producing pyloric obstruction by the use of ligatures.

THE SHORT ESOPHAGUS:

Peptic esophagitis naturally brings up the subject of the "short esophagus". Congenital short esophagus and the partial thoracic stomach resulting therefrom is, fortunately, not common. When present, the same increased tendency for regurgitation into the esophagus exists since the sphincter action of the diaphragm is absent. Acquired "short" esophagus is more common. When diagnosed preoperatively, it is frequently not found at surgery as the apparent shortening is commonly a manifestation of spasm of the esophagus. The relaxing effect of the anesthesia allows the esophagus to assume its true length. In experimental animals, Dey and his associates

(9), in 1946, produced spastic shortening of the esophagus by stimulation of the vagus nerves, manipulation of the stomach, liver and other abdominal viscera. Distention of the gallbladder also acted similarly. However, permanent acquired shortening of the esophagus can occur if the shortening due to spasm has been chronic. This may explain cases of true acquired shortening of the esophagus associated with some hiatus hernias. The increased difficulty at surgery is obvious.

PATHOLOGY:

Vinson and Butt² describe the pathology seen in their series of 215 cases of esophagitis obtained by post-mortem studies. In 163, or 76.5%, there was acute ulcerative esophagitis. There was loss of epithelial cells. The muscularis mucosa, when remaining, was infiltrated to varying degrees of neutrophils. This inflammatory reaction may extend to the submucosa and muscularis. The mucous glands were dilated due to blockage of the ducts. Hyperemia with or without thrombosed vessels was present in the mucosa. Pseudomembrane was present in 12½%. In 1% there were abscesses in the outer fibrous coat. Of the 213 cases, 4.5% revealed subacute ulcerative esophagitis. The predominating cells were lymphocytes, plasma cells, eosinophils, and fibroblasts. In the cases of chronic esophagitis, there were varying degrees of fibrosis. Post-mortem digestion was not believed to have produced the above-mentioned varying degrees of pathology.

DIAGNOSIS:

After the clinical syndrome of "heartburn" appears, diagnosis is usually made on the basis of the location and character of the distress. The complaint is a steady burning type of discomfort at the region of the xiphoid process. The discomfort is higher than that seen in gastric or duodenal ulcer and with usually slower and less relief from food or alkalis. In refractory or complicated cases, x-rays and esophagoscopy are indispensable. As mentioned before, the special value of endoscopy is demonstrated by the fact that the earlier case series were reported by esophagoscopists. Clinically, spasm of the lower esophagus is sometimes confused with angina. This is especially so when frank pain occurs instead of heartburn. In severe cases the pain reference may be to the neck or even the arms. Olsen⁶ states that pain is more likely to be with

radiation when it is the result of diffuse esophageal spasm.

TREATMENT:

In many, preventive measures are adequate. Such would include control of hiccups, frequent belching, psychoneurotic habits, unnecessary cough, straining at stool, irritating foods and medications, alcoholic excesses, etc. Irritation by prolonged presence of indwelling gastric tubes, duodenal tubes, etc., must be considered. Experiences with this patient stress the importance of bland foods, a Sippy regime, and sleeping in a semi-erect position. These will prove helpful in other cases in which regurgitation esophagitis is sufficiently important. Less exacting programs will suffice in milder cases. Since the heartburn and other substernal forms of discomfort caused by regurgitation esophagitis do not respond as quickly to anti-acids as do the symptoms of uncomplicated subdiaphragmatic peptic ulcers, lozenges containing anesthesin or orthoform may be helpful. Aluminum hydroxide or phosphate preparations will help not only by being acid buffers but also by their astringent effects. Bismuth subcarbonate or the periodic use of olive oil have their advocates. Belladonna and mild sedation will help some. In cases with severe pain, opiates will be necessary for a while. The possibility of habituation must be considered. Stenotic areas that remain bathed by gastric regurgitation or which are traumatized by the passage of food may respond to dilation. If not, surgery may be necessary, as also it would be for diverticula that trap the regurgitated material. Occasionally, gastrostomy is required to give adequate rest to the esophagus. Partial pyloric obstruction may require surgery. The relief of complete pyloric obstruction, when present, is obviously necessary for nutrition. With obstinate cases of esophageal ulcers, vagotomy with gastro-enterostomy, a resection of the stomach or resection of the esophageal lesion may be indicated.

OTHER FORMS OF ESOPHAGITIS:

Regurgitation esophagitis is the commonest type of esophagitis. Esophagitis of other etiologies include:

1. Caustic esophagitis, acid or alkali.
2. Foreign body irritation esophagitis.
3. Esophagitis associated with central nervous system lesions.
5. Stasis esophagitis

- 6. Esophagitis by extension of neighboring disease
- 7. Arteriosclerotic esophagitis
- 8. Curling ulcers in the esophagus in burn cases
- 9. Esophagitis due to virus, fungi, yeast, etc.
- 10. Rare esophagitis such as in scleroderma, etc.

COMMENT:

The stenosis in the case reported as not due to regurgitation esophagitis, However, regurgitation esophagitis with or without ulcer formation can go on to astenosis.

CONCLUSION:

- 1. The frequency of regurgitation esophagitis is such as to warrant more consideration by the medical profession.

- 2. The term "heartburn" is misleading and therefore is not desirable. The term "regurgitation esophagitis" is hereby recommended.
- 3. Esophagoscopy is worthy of more utilization now that safer instruments are available.

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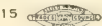
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gastric ulcer and duodenal ulcer as rather distant cousins and not as locational variants of a single disease. Justification for this attitude lies not only in the differences in treatment of choice and in response to various forms of treatment but also in an increased awareness of the physiological differences between the two conditions. Surgical resection for uncomplicated gastric ulcer is commonly advised now partially because of the difficult diagnostic differentiation from early cancer but also because of the extremely satisfactory long term results of such treatment. This is in contradistinction to duodenal ulcer in which situation the problem of anastamotic marginal ulceration is a serious one. The difference is likely related to the fact that gastric hypersecretion is usually marked in the patient with duodenal ulcer and seldom present in the patient with gastric ulcer.

The question of etiology of peptic ulcer remains poorly understood. There is unfortunately no satisfactory way of recognizing the individual who is going to develop ulcer. In view of the strong tendency to recurrence which exists there must be some significant physiological aberration. The present attitude towards etiology may be summed up by the presumption of an underlying or predisposing factor of chronicity which predisposes the individual to the development of ulcer and operates to prevent its complete and permanent healing. Superimposed upon this situation the facts at hand require an acute precipitating event which initiates the chain of events leading to a chronic ulcer.

Editorials

PEPTIC ULCER

The changing seasons highlight again the problem of peptic ulcer. It is of interest to review the changes in professional viewpoint which have occurred during recent years in regard to this important disease.

Perhaps the most interesting change in concept has been the trend towards considering

The field of diagnosis has shown no major change during the past decade and the procedures of value may be listed in this order:

1. History
2. X-ray examination
3. Gastroscoy (for Gastruc Ulcer)
4. Therapeutic Trial.

It would appear that diagnostic X-ray methods for peptic ulcer have reached the ultimate in their refinement and that there is a tendency to expect more from the method than it can conscientiously contribute. There is only one direct X-ray sign of uncomplicated peptic ulcer, the demonstration of a niche or crater. This is the only finding of value in the diagnosis of gastric ulcer. In duodenal ulcer the niche cannot be regularly exhibited. Here often the diagnosis must depend on the demonstration of a more or less typical contractural deformity. While accurate statistics regarding this problem are difficult to obtain Ivy and his coworkers state that from 5 to 10% of gastric ulcers and from 10 to 20% of duodenal ulcers cannot be demonstrated by X-ray. If careful study of a patient's history is made and found to be suggestive of peptic ulcer cases with negative X-ray studies should be given a therapeutic trial. A tentative diagnosis can often be made upon the basis of such a trial. From a diagnostic standpoint the chief problem of the clinician lies in the interpretation of an equivocal X-ray report of ulcer in a patient who does not have the symptoms of ulcer. The radiologist can prevent much diagnostic confusion by reporting his studies as: (1) showing peptic ulcer (2) as showing definite X-ray evidence of peptic ulcer, or (3) requesting reexamination.

The treatment of gastric ulcer in good risk cases is gradually shifting in the direction of subtotal gastrectomy for the reasons mentioned above. The treatment of uncomplicated duodenal ulcer has progressed in few details since the day of Sippy and in some respects has regressed. Certainly the meticulous attention to patient cooperation and the precise control of hyperacidity and secretion which Sippy taught are not often enough a feature of modern practice. To those who have observed the coming and going of the multitudinous shortcuts proposed for the treatment of duodenal ulcer such as larostidin, gastroenterostomy, vagotomy, and enterogasterone to mention a few, the future of

the new drug banthine will be watched with interest. It apparently is quite a potent drug and worthy of clinical trial but time and unbiased observation will be needed to evaluate its true worth. For the present at least the treatment of choice in uncomplicated duodenal ulcer continues to be a careful dietary program of the Sippy type with physical and mental relaxation during the period of healing combined with the judicious use of antispasmodics preferably belladonna and antacids, the amount and type of which to be determined by the degree of hypersecretion present and the bowel status of the individual case.

CONTRIBUTORS

The Editor sincerely solicits contributions of scientific articles for publication in *Arizona Medicine*. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the *Journal of the American Medical Association*. (See *Medical Writing* by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and *double-spaced*.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

WHAT DO YOU THINK?

Emanating from the Third National Medical Public Relations Conference on a county medical society level held in Cleveland, Ohio, December 3 and 4, 1950, the PHYSICIAN-SOCIETY was requested to answer the following questions as to "physician-patient" relationship, the keystone to a successful public relations program urged for accomplishment during the year 1951.

1. Is 24 hour emergency service maintained in your community?

Do you care for your patients when they call you at 2:00 a.m.?

Do you have emergency telephone service at your hospital?

2. Do you comply with and help maintain the local fee schedule?

Do you itemize your statements?

Do you explain your charges FIRST instead of after doubt arises?

Do you accept as payment in full checks from insurance cases where additional charges on your part would work a hardship on the insured?

Do you discuss these problems with NEW MEMBERS of your society to assist them in getting acquainted with local custom?

3. Do you read "The Principles of Medical Ethics" and your Constitution and By-Laws?

4. Does your county medical society or state association have a "Grievance Committee" that really functions?

5. Do ALL THE PEOPLE IN YOUR COMMUNITY receive medical care? Do you encourage new residents to select a "family physician" before illness strikes?

IF GOOD PUBLIC RELATIONS BEGIN AT HOME, what does your reception room look like?

Letter to the Editor

November 3, 1950

Frank J. Milloy, M.D.
Editor, Arizona Medicine
401 Heard Building
Phoenix, Arizona

Dear Dr. Milloy:

In the personal note of the Arizona Medicine for October 1950, I noticed a note that I had just completed a year's residency in cancer surgery at the M. D. Anderson Hospital in Houston, Texas.

This is not entirely correct, and while no retraction is needed for what you have said, I wish that you would publish the correct information in the same column in the near future.

The correct information is that I have just returned to practice after an absence of sixteen months; one year of which was spent as a fellow in malignant disease at the M. D. Anderson Hospital for cancer research and the University of Texas Post Graduate School of Medicine in Houston. This time consisted of four months being spent on tumor pathology, four months being spent on radium and X-ray therapy and four months being spent on general tumor surgery. So as you see, this was not a residency in cancer surgery. Following this, I was staff surgeon at the University of Texas Post Graduate School of Medicine, M. D. Anderson Hospital for Cancer Research, being in charge of the head and neck tumor surgery at that institution for four months.

I wish to thank you for your attention to this matter and for a publication of the correct statement.

Very truly yours,

JAMES M. OVENS, M.D.

EXECUTIVE SECRETARY'S REPORTS

REPORT ON THE THIRD ANNUAL PUBLIC RELATIONS CONFERENCE

Dr. Elmer L. Henderson, President of the AMA, in his salute to county medical societies during the opening two-day session of the Third National Medical Public Relations Conference held in Hotel Statler, Cleveland, Ohio, December 3 and 4, 1950, stated: "The quickest way to eliminate threats to the American Medical Profession is to meet the people's need for adequate care at a price they can afford to pay"

and whether intentional or not struck the keynote to what in my observation became or was the most widely discussed topic of the conference. Dr. Henderson emphasized: "Positive action for the public good is the essence of successful public relations."

Louis B. Seltzer, Editor of the Cleveland Press and one of the principal speakers at the conference banquet, stated: "The family physician

of past years had the world's finest public relations without knowing it. Public relations must be added to the growing list of medical specialties" and he cautioned the group that "it could not afford to protect the doctor not true to the highest ideals of the medical profession and urged it to recognize that the subject of medical care is not the exclusive domain of the medical profession."

Dr. John W. Cline, President-elect of the American Medical Association, in his address before the assembly emphasized that the doctor can best serve his profession through good physician-patient relations. This can be achieved through proper education of the profession itself, handicapped only by those members who are inactive and do not take part in county and state programs. Summarizing, the most prevalent complaints of today are (1) excessive fees, (2) inavailability of medical care, (3) the practice of rebates, and (4) gentlemanly conduct. To further improve public relations the physician is encouraged to take an active part in civic enterprise and strive to improve press relations through periodic physician-press conferences. State Associations must display leadership to their component county societies and likewise, the AMA must continue leadership and cooperation among its constituent bodies thereby more firmly cementing its ties and prepare for the future.

Dr. Cleo M. Miller, President of the Nashville (Tennessee) Academy of Medicine, presided as Chairman over a panel discussion on laying the ground work for a successful public relations program. Participants were Dr. Russell B. Roth, Secretary of the Erie (Pennsylvania) County Medical Society; Mr. Arthur P. Tiernan of Evansville, Indiana, Executive Secretary to the Vanderburg County Medical Society; Mr. Henry S. Johnson, Executive Secretary of the Medical Society of Virginia; Dr. Charles S. Lakerman of Rochester, New York, Chairman of the Public Relations Committee of Monroe County Medical Society; and Dr. R. B. Chrisman of Miami, Florida, Secretary of the Dade County Medical Society. It was quite evident from the discussions presented by these able speakers that the first requisite to a successful P/R program is the full and enthusiastic participation of the medical profession itself. One could readily understand the success achieved in these states through organization and a determination to

bring medicine's story to the people through deeds and not words. Among the most notable accomplishments were the establishment of county medical Service Bureaus providing medical care for all on a 24-hour basis, including provision for an effective emergency call system; operation of grievance committees either on a state or county level with emphasis on granting such committees adequate disciplinary authority; support of all voluntary health insurance plans and provision for a schedule of regular monthly payments for those patients who are uninsured; establishment of an effective speakers bureau capable of discussing both medical and social subjects with availability on short notice; continuation of a well balanced radio advertising program and establishment of proper training for members of physicians' staffs in the art of building daily good physician-patient relations.

Mr. Rollen W. Waterson of Oakland, California, Executive Secretary of Alameda County Medical Society, presided as Chairman over a panel discussion on Activities With a Purpose. Speakers were Dr. Eugene A. Ockuly of Toledo (Ohio) Academy of Medicine; Dr. Fred Sternagel of West Des Moines, Iowa, Chairman of the Committee on Medical Service and Public Relations of the Iowa State Medical Society; Dr. E. L. Bernhart of Milwaukee, Wisconsin, President of the Medical Society of Milwaukee County; Dr. William M. Skipp of Youngstown, Ohio, representing Mahoning County Medical Society; Dr. Carl H. Vohs of Clayton, Missouri, President of the Missouri Medical Service and former President of the Missouri Medical Association; and Dr. Frederick B. Davies of Scranton, Pa., representing the Committee on Emergency Disaster Medical Service, Medical Society of the State of Pennsylvania. This discussion in effect re-emphasized the importance of active participation in those fundamentals hereinabove outlined as representative of the ground work of a well rounded P/R program, each being considered an essential part of the over all pattern. The scope of activity in each field must of necessity be developed around the individual community need, however, there can be little doubt of such need.

Possibly the words of Dr. Carl H. Vohs of the Missouri Medical Service speaking before some 375 members of the AMA Public Relations Conference may best sum up the intense interest

and seriousness of its deliberations when he stated: "As long as any but indigent Americans do not have adequate health insurance, the danger of Socialized Medicine remains with us. It may seem like the medical profession has convinced the people of the folly of State Medicine and that private medicine serves them best—especially after the last election—but this is only a truce, a breathing spell to complete our job. With the world situation as chaotic as it is, the American people seem ready to submit to any controls or regulations and that they may become accustomed to allocations and regulations from government. That is one of our dangers. The other is inertia within our own profession. With many of our members going into the service those remaining will be over burdened trying to care for the people and will rely on the National and State Associations pushing the fight. But the fight must be won on the local community level. Approximately 70 million people now are covered by some form of hospital insurance and 40 million by some surgical

plan. I urge the doctors not to rest until every community has such protection. The American people will have health insurance through us or through the government."

The announcement by Dr. Louis H. Bauer, Chairman of the Board of Trustees of AMA, at a dramatic, early morning meeting of the House of Delegates held December sixth, that it had appropriated \$500,000.00 out of its National Education Campaign Fund, raised to defend medical freedom, for the aid and support of medical schools in need of additional financing, was a realistic blow to federal subsidies and received unanimous approval. It is the hope that this will start a chain reaction and become a stimulus to physicians and other professions, industries, businesses, labor groups and private donors to contribute to this very important cause of protecting and advancing the interests of medical education and the public health.

Respectfully submitted,

ROBERT CARPENTER,

Executive Secretary.

REPORT ON THE NATIONAL EDUCATION CAMPAIGN CONFERENCE OF THE AMERICAN MEDICAL ASSOCIATION

The Third Annual Conference of the National Education Campaign of the American Medical Association met in joint session with the House of Delegates in the Grand Ballroom of Hotel Statler in Cleveland, Ohio, December 7, 1950. Dr. Elmer L. Henderson, President and Chairman of the Campaign Coordinating Committee reviewed legislation affecting medicine and Dr. John W. Cline, President-elect, reported on the results of the doctors' campaign on public thinking.

I think to counteract some of the fantastic claims of our opponents relating to expenditures by AMA during its gigantic advertising campaign in October of this year, it might be well for all of us to review the facts. The total expenditure born by the doctors for this purpose was \$1,100,000, reaching an audience through the media of 10,300 newspapers and Sunday supplements with a circulation of 115,630,487; 55 national magazines with a circulation of 55,202,080 and 1,600 radio stations reaching an estimated 108,205,034. The total number of individual advertisers taking part who bought space in their local newspapers or time on radio stations expressing their conviction that the vol-

untary way is the American way was 65,246, subscribing to a total of 1,186,594 inches of newspaper advertising space and spent a total of \$2,019,849, including 35,362 radio spots, direct mailing, posters, billboards and television programs, which is, of course, exclusive of the amount spent by the doctors and represented their voluntary contribution in behalf of American Freedom.

Dr. Ernest E. Irons, Past President of the AMA, spoke on "The Challenge Ahead," followed by an address on "The Public Significance of Medicine's Advertising Campaign" by Leone Baxter, General Manager of the National Education Campaign.

Dr. R. B. Robbins, Vice-President of AMA, was moderator of a panel talk on "State Participation in Medicine's National Campaign" by James A. Waggener, Field Secretary, Indiana State Medical Association; Leo Brown, Public Relations Director, Pennsylvania State Medical Society; Charles Lively, Executive Secretary, West Virginia State Medical Association; and M. C. Smith, Executive Secretary, Nebraska State Medical Association. Following was an address by Clem Whitaker, Director of the Na-

tional Education Campaign, on "Medicine's may be briefly summed up in two major points, (1) to continue unrelentingly the endorsement drive, and (2) seek the understanding, cooperation and support of labor to join the ranks of those opposed to the further socialization of our country and for the restoration of the American Way of life.

As a dramatic step toward this end an address by William L. Hutcheson, General President, United Brotherhood of Carpenters and Joiners of America and Vice-President of the American Federation of Labor, entitled: "Socialized Medicine Is No Bargain," was delivered. It was stated that at its general convention recently held a resolution supporting the National Health Program was voted down by some 300 delegates representing better than 54% of the total membership. Mr. Hutcheson concluded "I have always

respected the medical profession for the fine contribution American medicine has made to human welfare. As I watched your battle against regimentation during the past two years, I have added to that respect. The physicians of this country have shown that they are willing to fight for their convictions. I salute you today not only as doctors, but as crusading citizens as well. We in the labor movement have our own cross of regimentation to bear. The fight you are making is part of the same war. It is a war against concentration of authority in a few hands in Washington. As a veteran of 40 years in the labor movement, I know what it is to fight for human rights. I am happy to take my stand beside you."

Respectfully submitted,

ROBERT CARPENTER,

Executive Secretary

**PHOENIX CLINICAL CLUB
MASSACHUSETTS GENERAL HOSPITAL
M.G.H. CASE No. 31102**

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A seventy-seven-year-old widow entered the hospital because of marked dyspnea, abdominal distention and tenderness in the right upper quadrant.

Nine years before admission she had a subtotal thyroidectomy for nontoxic goiter, 140 mg. of tissue having been removed. The pathological report was "hyperinvolution." After recovery she lived at a home for aged women, where her activities were limited. Five years before admission she received some medical attention for "gall-bladder trouble" and "a heart condition." She had at that time only shortness of breath and could not take digitalis because this caused vomiting. She spent nine weeks in bed and was well thereafter. Three months before admission she began having pain in the right upper quadrant, which came on only after lying in bed. This pain lasted up to two hours, varied in severity and had no relation to food or exertion. Long-

standing constipation became accentuated and required an additional laxative tablet each day. Four days before admission she entered the Emergency Ward because of painful migratory arthritis involving both feet and the right hand. Physical examination at that time and X-ray study were consistent with rheumatoid arthritis. She was discharged to the Out Patient Department. One day before admission, distention of the abdomen began after an unsuccessful enema had been given and the patient's dyspnea increased. Repeated enemas resulted in several loose movements, without relief of the distention or the dyspnea. On the day of admission she had two episodes of vomiting.

Physical examination revealed a dyspneic woman in moderate discomfort but without pain. The lips, ears and mucous membranes were cyanotic. The heart was not enlarged, and the sounds were normal. The neck veins were slightly distended and pulsating. Bilateral crackling basal rales were heard, and in the same areas there was increased dullness to percussion. There was no peripheral edema. The abdomen was markedly distended and tympanitic. Peristalsis was diminished. There was tenderness in the right upper quadrant. No abdominal splinting or masses were noted. Rectal examination was negative. The rectum was filled with soft,

tan feces, which were guaiac negative.

The rectal temperature was 100°F., the pulse 84, and the respirations 20. The blood pressure was 168 systolic, 80 diastolic.

Examination of the blood revealed a red-cell count of 3,800,000 with 10.5 gm. of hemoglobin, and a white-cell count of 16,000 with 91 per cent neutrophils. The urine was acid and had a specific gravity of 1.016, with a four plus test for albumin and occasional white cells and casts. The Bence-Jones protein was negative. The serum nonprotein nitrogen was 42 mg. per 100 cc., and the total protein 5.8 gm., with an albumin-globulin ratio of 1.1. The carbon dioxide and chloride levels were normal. The phosphorus was 1.4 mg. per 100 cc., and the alkaline phosphatase 10.6 Bodansky units.

X-ray films of the chest showed mottled areas of increased density scattered throughout the lungs. The vascular shadows were increased in size. The heart was prominent in the region of the left ventricle, and the aorta tortuous. Films of the abdomen showed considerable gas in the small and large bowel, neither of which appeared to be dilated. There was a laminated gallstone in the region of the gall bladder. No abnormal soft-tissue masses were seen. An electrocardiogram showed normal rhythm at a rate of 75, a PR interval of 0.16 second, a flat T₁, upright T₂ and T₃ and a diphasic T₄, with a sagging ST₄. The patient was digitalized with Cedilanid and was given sulfadiazine. On the second hospital day the patient was considerably improved and was no longer orthopneic, dyspneic or cyanotic; the lungs had cleared but a few patches of fine rales persisted at both bases posteriorly. The abdominal distention was diminished, and the two masses in the right upper quadrant could be felt 5 to 7 cm. below the costal margin. These were not tender and descended with inspiration; they were thought to be due to a coarsely irregular liver edge. The sulfadiazine level was maintained at about 10 mg. per 100 cc., with an intake of about 1250 cc. and an output of about 1000 cc.

At 12:30 a.m. on the fifth hospital day she had an episode of steady precordial pain with gradual onset. Moderately severe orthopnea, with a respiratory rate of 40, lasted for about twenty minutes. Repeated electrocardiograms showed inverted T₁, T₂ and T₃ and a sagging of all ST segments. X-ray films of the chest on the same day showed that the mottled areas of increased

density previously described had cleared considerably. Only moderate congestion of the vessels was noted, and no infarcts were seen in the posteroanterior view. The nocturnal dyspnea recurred during the succeeding two nights. There was no increase in the pulmonary rales.

A bomsulfalein test on the fifth hospital day, using 5 mg. of the dye per kilogram of body weight, showed 80 per cent retention in forty-five minutes. A van den Bergh test was normal. An aspiration biopsy of the liver showed no abnormality. The cephalin flocculation test was one plus in forty-eight hours. A barium enema was negative.

The white-cell count rose steadily and reached 31,400 on the eleventh hospital day, with 75 per cent neutrophils, 5 per cent lymphocytes, 4 per cent eosinophils and 16 per cent large monocytes. A low-grade fever (99 to 100°F.) and anemia persisted. The stools were brown and formed. The urine persisted in showing a three plus to a four plus test for albumin and a specific gravity of 1.006 to 1.020.

On the twelfth day the patient suddenly had an attack of acute pulmonary edema, for which she was treated with tourniquets, morphine, Cedilanid and, finally, venesection. She rallied but developed peripheral edema. She became incontinent, with slowly increasing depression and unresponsiveness, and died on the twenty-third hospital day.

DR. M. W. MERRILL

We are considering today a most interesting clinical problem. That of a 77 year old widow who was admitted to the hospital acutely ill, and died 23 days later.

The past history is of some value in the discussion. She had a non toxic goitre removed nine years before admission, was known to have chronic gall bladder disease, and five years previously had been in bed nine weeks, apparently from some type of cardiac disease. This was characterized by shortness of breath and inability to tolerate Digitalis. The patient apparently made a good recovery from the illness, remaining well until 3 months before admission. During this 3 months period prior to entry, constipation increased pain which came on while prone, located in the right upper quadrant, developed and the patient began to suffer from what was apparently an acute rheumatoid arthritis. The day before admission the patient began to develop abdominal distension and dyspnoea follow-

ing an enema. Successive bowel irrigations produced loose bowel movements, but failed to relieve the distension or shortness of breath. On the day she entered the hospital the patient vomited several times.

On admission the patient was dyspnoeic and cyanotic, uncomfortable but in no severe pain. Abdominal distension was marked and bowel was tympanitic with diminished sounds. The heart was not enlarged, but the neck veins were distended and pulsating indicating some pulmonary hypertension. Rales and areas of increased dullness were noted in the chest. There was tenderness in the right upper quadrant, but no masses were felt in the abdomen. Rectal examination was negative. The temperature on admission was 100 degrees rectally, the pulse 84, the respirations 20, the blood pressure 168/80.

The laboratory work showed a leucocytosis of 16,000 with a predominance of neutrophils, 91%. The urine contained albumin, casts, white blood cells but no Bence-Jones protein. The NPN was mildly elevated to 42 mgms. and the total serum protein was 5.8 grams, very slightly under the lower limit of normal. There was a tendency toward the reversal of the A/G ratio. The carbon dioxide, chlorides, phosphorus were all normal, but the alkaline phosphatase was elevated to 10.6 Bonansky units.

The chest X-ray on admission showed mottled areas of increased density throughout the lung with some increase in the vascular shadows. In the physical examination the heart was reported as not enlarged and the X-rays showed only a prominence in the region of the left ventricle. I take it from this that the heart was actually not much enlarged and believe that this is an important finding in the differential diagnosis.

The films also showed gas in both the large and small bowel and apparently without much dilatation. This must be considered as an ileus and not as an obstructive phenomenon. There was also a large laminated gall stone visible but no abnormal soft tissue masses could be seen.

Electrocardiographic tracing with a flat T₁ indicated most likely an old coronary occlusion. We are probably justified from these findings in concluding that the cardiac disease five years before was probably on this basis.

After admission to the hospital the patient responded well to Sulfadiazine and Cedalanid. The dyspnoea and orthopnoea disappeared, and she was no longer cyanotic. The abdominal disten-

sion went down and two masses became palpable in the right upper quadrant. These were non-tender, decreased with inspiration and were felt to be due to liver enlargement.

One should probably stop at this point and try to analyze just what was going on when the patient entered the hospital. However I think it may be preferable to complete a summary of the clinical course. On the 5th hospital day she developed steady precordial pain with some orthopnoea for a while and increased respirations. E.K.G.s were taken serially and showed an inversion of T₁, T₂ and T₃ and a sagging of all of the SD segments. This probably indicated multiple infarctions or a laterally placed lesion. Acute pericarditis must be thought of in connection with these findings, but here the SD segments should remain elevated. The X-rays were again repeated and showed considerable clearing of the mottled densities and no evidence of pulmonary infarction. There was no increase in the pulmonary rales. Remainder of her clinical course was characterized by the development of an acute left ventricular failure on the 12th hospital day, the development of a peripheral adema, and the gradual decline to death on the 23rd day.

Attention should be called to several of the other laboratory findings. Of most importance was the steady climb of the white blood count to 31,400 with 75% neutrophils, 5% lymphocytes, 16 monocytes and 4% eosinophilia. The latter point may help in the differential diagnosis. Fever was never prominent throughout the course of the illness, anemia remained present, the stools were brown and formed, and the urine consistently ran a 3 to 4 plus test for albumin.

A liver biopsy was done and the tissue obtained was normal. On a brömsulphalein test, 80% retention in 45 minutes indicated a chronic liver disease, and the cephalin flocculation test, 1 plus in 48 hours, indicated no hepatic process.

Colon X-rays were normal and apparently a G.I. Series was not done.

In attempting to diagnose this patient's basic pathology, consideration must be first given to her cardiovascular system. Was she in cardiac failure on admission? She was cyanotic, dyspnoeic and orthopneic. However, much of this could have been due to the patient's distension and we must remember that this was bowel distension and not ascitic fluid. Part of her respiratory difficulties probably were due also to pul-

monary findings which suggested a patchy pneumonitis of a rather acute character. The subsequent rather rapid clearing of the lung fields bear this out. In the absence of cardiac enlargement, peripheral adema or ascites, and with a pulse of 84 and a normal blood pressure, I think that we must consider that cardiac pathology was not the primary cause of her trouble on admission. A circulation time would have been of great value here. Later however, I feel sure that she developed probably a coronary occlusion with infarction and subsequent ventricular failure which ultimately led to her demise. I rather think that the Sulfadiazine with its action on the pneumonitis contributed more than the Cedalanid to her progress the first few days of her admission.

Was there some acute or chronic intra-abdominal condition behind a lot of this patient's difficulty? We know she had a chronic gall bladder disease with at least one calculus, but nothing indicated that she had an acute cholecystitis. In this connection, pancreatitis in a chronic recurring form must be thought of. Inasmuch as there was no abdominal pain and her abdominal symptoms and distension subsided rather quickly, and in the absence of any confirmatory laboratory work, I am inclined to disregard this as much of a factor.

What about this patient's liver—how much did it contribute to her clinical picture. We pretty well know that it was not the seat of an acute process. She had no jaundice, stools were not acolic and cephalin flocculation did not indicate an acute condition. On the other hand, we are fairly certain that she had a chronic liver disturbance. The bromsulphalein retention test, the apparent liver enlargement, the lowered serum protein, the tendency to inversion of the A/G ratio, and the moderate increase in the alkaline phosphatase activity all point to a chronic liver disease. What this was is not clear. The liver biopsy did not help. Apparently it was not on a chronic congestive basis. I cannot rule out metastatic malignant infiltration. This could have been missed in the biopsy. Primary carcinoma must also be thought of, but this could hardly have been in the ductless system with no evidence of jaundice. A chronic hepatitis, or possibly a cirrhosis should be considered, but one would think that the liver biopsy would have established whether either of these diagnosis. I believe the palpable abdominal masses were

probably liver or liver and gall bladder. In the presence of a calculus, a large, distended palpable gall bladder is a possibility. The possibility of this being a carcinoma of the gall bladder must also be strongly considered. In the absence of a G. I. Series, or symptoms suggesting gastrointestinal disease, we must conclude the palpable masses were probably not in the stomach or the bowel. As noted, the barium enema was negative. Also we must keep in mind that these masses moved down with respiration which would rule out retroperitoneal lesions. Renal tumor must be considered, but the mass was intraabdominal, below the costal margin, and not in the flank. No I.V. Pyelogram is reported.

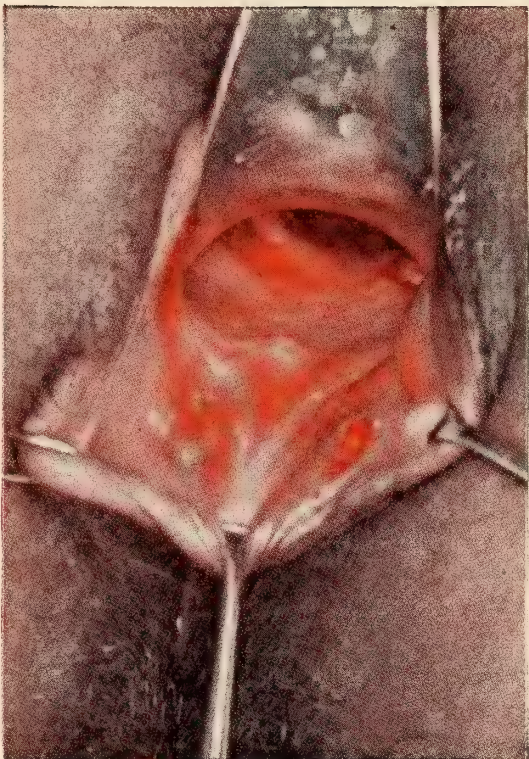
The blood picture is somewhat confusing. I can readily explain the moderate degree of secondary anemia which persisted throughout her illness on the basis of age and nutritional deficiency. The white blood picture is a different matter. The pneumonitis, if such it were, on admission could well have been behind a 16,000 count but what was behind the elevation to 31,400 with 75% polys and including 4 eosinophiles? No mention is made of chills or a high temperature elevation to indicate an abscess or other severe suppurative infection. The picture is not that of a leukemia with a preponderance of polymorphonuclears. Another point is the eosinophilia. This is not high but definitely present. The unusually high white count even the normally present eosinophilia disappears, but in this case it comes on after the patient's admission to the hospital and despite a steadily rising white blood count. One wonders if any of the treatment given could have been a factor.

While discussing the eosinophilia, one must consider parasites, but I will mention them only to say that there is nothing in the information given to substantiate this diagnosis.

In a generalized carcinomatosis a white blood count is often seen. I do not believe that it is possible to rule out a malignancy in this case. Neither do I believe that it is possible to localize it even if it be present. I strongly suspect that if it is present it is in the right upper quadrant of the abdomen and possibly in the gall bladder. We have considered the G. I. System, the hepatic system, and have mentioned renal tumors. There is no substantial evidence pointing to an accurate localization in any of these structures or in the skeletal structures. We must also consider the pulmonary findings: mottled areas of increased



a. Ulcerative amebiasis during Diodoquin therapy. In this patient with severe hemorrhage, edema and necrosis, the ulcers show healing, with many scars. No active lesions are seen.



Photographs courtesy of Louis H. Block, M. D., Chicago

b. Three months later, after continuing Diodoquin therapy, extensive scarring indicates healing. Inflammation is further reduced and only superficial areas of inflammation remain.

AMEBIASIS: "Diodoquin is probably the least toxic of the drugs and contains the most iodine."¹ "Diodoquin now appears to us to be the drug of choice [for outpatients] because of its effectiveness and because it is tolerated well by most patients."²

In acute or latent forms of amebiasis, Diodoquin® (diiodohydroxyquinoline) the potent amebicide, may be administered in large dosage over prolonged periods. Diodoquin contains 63.9 per cent of iodine...is tasteless...relatively nontoxic...orally administered.



1. Johnson, S. K.: Mississippi Doctor 27:69 (July) 1949.
2. Merritt, W.: J. Florida M. A. 35:351 (Dec.) 1948.

density on admission. These subsided to a considerable extent rather rapidly, probably because of the chemotherapy. This does not sound like malignant invasion of the lungs, and neither does the X-ray description. However, neither does it definitely rule it out.

I believe we must seriously consider periarteritis nodosa as a principal factor in this patient's illness. This condition is being recognized more and more frequently as its relationship to Sulfa sensitivity has been well established. In our case it could account for many of the findings. The renal picture with the continual finding of urinary albumin could be explained on the basis of involvement of the renal arteries by this process. Some type of a chronic nephritis was present and periarteritis nodosa is a possibility. The abdominal distension in the patient had on admission possibly was aggravated by this process in the mesenteric vessels. Surely the distension was not produced by the actual mesenteric thrombosis, recovery was too quick for this to have been the case. Could not the coronary accident have been the result of periarteritis nodosa? It is not well known that this pathological process when it involves the coronary vessels can lead to a vascular occlusion and infarction.

The confusing white blood count and the eosinophilia and the absence of a high temperature, chills and other evidence of a suppurative process can be explained on the basis of the inflammatory reaction of a widespread endarteritis. The eosinophilia which made its appearance could easily have been caused by an exacerbation of this disease. One must also consider the elevation of the white blood count which follows coronary occlusion. I am assured that it is in massive occlusions, this elevation might be present on the second day, but very unlikely to climb to 31,000 six days after the accident as is noted in the protocol. Neither can an occlusion with an infarction explain the appearance of the eosinophiles.

I would like to submit this for your consideration. The elderly lady was admitted with distension and a pneumonitis. Sulfadiazine was vigorously administered and five days later her lung findings were better. However, she develops a coronary and seven days after this she goes into an acute cardiac failure. She then goes steadily down hill and dies. If she had a periarteritis nodosa on admission to do a previous sulfa

sensitivity, and who might not have in this day of chemotherapy, the administration of further sulfa might well have produced an acute inflammatory exacerbation of the process. My first diagnosis will then be coronary occlusion with infarction and subsequent cardiac failure, and a chronic nephritis with periarteritis nodosa as the basic pathology. Secondly, generalized carcinomatosis, the primary seat of which is unknown with gall bladder being a possibility.

DIFFERENTIAL DIAGNOSIS

Dr. Reed Harwood: Whatever else we are dealing with in this case it is evident that the patient had congestive heart failure. I think that two questions should be considered—first, the type of heart disease that was responsible for the failure and, second whether any further disease contributed to her death.

Nine years before admission she had a subtotal thyroidectomy. This raises the question of myxedema. If she did have myxedema it is not evident from the record.

Four days before admission she came to the Emergency Ward, complaining of painful migratory arthritis. It is unusual but not impossible to see acute rheumatic fever in a person of this age; I have seen it in persons of fifty years. One would expect, however, to find an increased PR interval in the electrocardiogram and to have more statements about her joints after she was admitted to the hospital.

The low-grade fever and the anemia suggest a subacute bacterial endocarditis, but I consider that as remote. She was an old woman who had a moderate hypertension. The X-ray films showed some enlargement of the left ventricle, and I think it is likely that she had hypertensive heart disease. At her age it is reasonable to expect that she had sclerosis of the coronary arteries. I suggest that she had a combination of hypertensive and arteriosclerotic heart disease.

The initial electrocardiogram was not strikingly abnormal, and I am interested to see if the changes that took place were consistent with an infarct. She was given digitalis, and we therefore expect to find sagging of the ST segments. I cannot say with complete confidence, however, that these tracings are consistent with an infarct. But since, following the attack of precordial pain, there was a definite change in CF₄, it seems extremely likely that she had a myocardial infarct.

In answer to the first question, that is, the type

of heart disease responsible for failure, I believe that she had hypertensive and arteriosclerotic heart disease, with a small myocardial infarction while she was in the hospital.

Did she have anything else that contributed to her death? She had abdominal pain and constipation shortly before admission; she was found to have a secondary anemia and a persistent 4 plus test for albumin, without striking abnormalities in the urinary sediment. The attending physicians evidently considered the possibility of multiple myeloma because of the marked albuminuria and anemia but the test for Bence-Jones protein was negative and the serum protein was not markedly increased. I do not believe that this entirely rules out multiple myeloma, but at least the evidence is against it. It was found that she had a phosphorus of 1.4 mg. per cc. and an alkaline phosphatase of 10.6 Bodansky units, both of which are abnormal figures. The only condition that I know of in which the phosphorus is reduced to such a low figure is hyperparathyroidism, but that may be ignorance on my part. If at post-mortem examination and adenoma of the parathyroid gland was found. I should be willing to give the opinion now that it did not contribute to her death. I am inclined to think that she did not have an adenoma, because there is so little evidence to go with it. The alkaline phosphatase was definitely increased, which suggests some disease of the bone in which the osteoblastic activity is increased. Once again one thinks of hyperparathyroidism, Paget's disease or some type of malignant disease involving the bone.

Another finding is the presence of two masses in the right upper quadrant. For lack of a better explanation I decided that she had a liver that was probably engorged from early right-sided failure of the heart and a chronically inflamed gall bladder. Both masses were rather low in the abdomen, at least four finger-breaths below the costal margin. She might conceivably have had a diseased kidney on that side.

We next come to the consideration of disease of the liver, about which there are many contradictory data. Evidently the attending physicians thought that she had liver disease. They did a bromsulfalein test on the day that she had acute left ventricular failure and found that she had 80 per cent retention. At the same time a van den Bergh test was normal. A biopsy of the liver was normal, and a cephalin flocculation test

was not definitely abnormal. The serum protein level and the albumin-globulin ratio were normal. With all this negative evidence I am going to disregard the bromsulfalein test or at least not give it undue importance. I do not know what happens to the bromsulfalein test in cases of congestive failure, but it is at least possible that during acute congestive failure more of the dye would be retained.

Finally, there was a peculiar reaction of the bone marrow, which had produced a leukocytosis by the twelfth hospital day. I should like to know about some of the other white-cell counts and differentials during the preceding interval.

Dr. Benjamin Castleman: On admission, the white-cell count was 16,000; subsequently, it was 13,000, 18,000, 23,000 and 31,000 on the tenth day it was 32,000 and then 18,000 and 32,000. In the differential counts the neutrophils ranged from 91 to 74 per cent, and then from 71 to 77 per cent.

Dr. Harwood: When did the monocytosis appear?

Dr. Castleman: On the tenth day, there were 5 small lymphocytes and 3 monocytes; on the fifteenth day, 5 small lymphocytes, 6 large lymphocytes and 3 monocytes; three days later, 4 large lymphocytes, 9 small lymphocytes and 8 monocytes with 2 myelocytes.

Dr. Wyman Richardson: There were numerous smears interpreted by different persons.

Dr. James A. Roth: The monocytes were not typical. They were large mononuclear cells, which I could not classify. They stained light blue.

Dr. Harwood: I should like to ask Dr. Schulz if there is anything in the chest plate to suggest any disease other than congestive failure.

Dr. Milford Schulz: The pulmonary markings are prominent. They do not look just like the prominent markings that are seen with lymphatic spread of a tumor. There is not much fluid in the chest. In the lateral view there is a triangular shadow in the posterior gutter that could indicate an infarct, but it is not entirely characteristic.

Dr. Harwood: Do you want to say anything about the bones?

Dr. Schulz: All the bones are decalcified but no more than one would expect in a person of her age. There is no evidence of cysts, and no change in the vertebral bodies. There are old

arthritic changes in the hands and feet. I do not see any localized areas of destruction.

Dr. Harwood: Is there anything suggestive of miliary tuberculosis in the lungs?

Dr. Schulz: The picture is not consistent with that of miliary tuberculosis. Lungs that look like this are disturbing. One thinks of passive congestion, early lymphatic spread of malignant disease, pulmonary fibrosis and even miliary tuberculosis; something similar is often seen in diseases like periarteritis nodosa.

Dr. Harwood: Do you see anything in the lungs that suggests the need for sulfadiazine? The temperature was 100°F. when the patient came in, and she had a high white-cell count. There is nothing in the record, however, to give me a clue why sulfadiazine was necessary, and this raises the question why patients have to be treated with some kind of chemical. We know that occasionally a fever subsides without their use, and I doubt that this patient needed sulfadiazine. I shall proceed, leaving that statement for what it is worth.

To go on with the discussion, I think that some other disease besides heart disease was found post mortem. I have no idea what, but the evidence points to a lesion that involved bone. I should think, first of all, of a malignant tumor with widespread metastasis, including involvement of the lungs. The original site of such a tumor I cannot determine. It may have been the thyroid gland, that gall bladder or some other intra-abdominal organ.

Another possibility is miliary tuberculosis. The evidence for this is not striking. I also thought of the possibility of some acute intra-abdominal catastrophe to explain the increasingly high white-cell counts, such as thrombosis or embolus of some vessel or perhaps perforation of the gall bladder. I remember a patient with carcinoma of the prostate who developed a high fever and chills. I thought that he had a kidney infection, but at post-mortem examination we found that the gall bladder had ruptured into the bed of the liver, discharging a hundred or more small stones. It was an entirely unsuspected finding. In the present case, I also thought of the possibility of disease in the liver. The likeliest lesion would be a metastatic carcinoma.

Dr. Richardson: I did not see this patient, but I did see a blood smear taken at about the midpoint of her illness. At that time she had re-

ceived sulfadiazine for some time. The picture was that of a considerable degree of leukocytosis. There was no evidence of infection from the smear. There were some peculiar cells, which might have been very immature red cells, and I thought that the whole picture might have been due to sulfonamide therapy. Sulfonamides had been stopped, however, a few days previously, but still the total white-cell count remained elevated. There was also red-cell regeneration. I wrote in my note that since the picture had continued after the stopping of sulfonamides it was quite consistent with involvement of the bone marrow, presumably by a malignant tumor that had also produced considerable anemia. There were no toxic changes such as are usually seen in uremia, nor was it hypochromic by measurement. It was a "simple anemia" but must be explained somehow.

Not knowing the answer in this case, I should say that the patient probably had malignant involvement of the bone marrow. The possibility of myeloma should be considered. Those queer cells might conceivably have been immature plasma cells.

Dr. Chester M. Jones: I should like to take minor exception to one statement that Dr. Harwood made, namely that an elevated phosphatase means disease of bone. That is not correct because an elevation of the phosphatase level may also occur in liver disease and may be as high or higher than that noted in involvement of bone.

Dr. Harwood: Is that true in patients without jaundice?

Dr. Jones: Yes.

Dr. Harwood was entirely right in stating that the elevation of the bromsulfalein retention could be explained by congestive failure. No doubt one could observe dye retention, positive cephalin flocculation and Takata Ara tests and at least some change in the albumin-globulin ratio as a temporary episode occurring with congestive failure. On the other hand, 80 per cent retention in forty-five minutes is extremely high.

I do not recall this case too well, since the patient came in at a time when I was out of the hospital for a few days. I do recall, however, that we entertained the thought of metastatic cancer of the liver as a real possibility and that is why the biopsy was done. The fact that nothing was found on aspiration biopsy is no proof

against its existence. One can miss a nodule very easily.

CLINICAL DIAGNOSIS

Metastatic carcinoma to lungs and liver?

DR. HARWOOD'S DIAGNOSES

Hypertensive and arteriosclerotic heart disease, with congestive failure.

Carcinoma of gall bladder or thyroid gland, with metastases to bone marrow.

ANATOMICAL DIAGNOSES

Carcinoma of gall bladder, with extension into liver and with metastases to lung, liver, peritoneum and bone marrow.

Cardiac hypertrophy, hypertensive type, slight. Cholelithiasis.

Hydrothorax, slight, bilateral.

PATHOLOGICAL DISCUSSION

Dr. Castleman: The post mortem examination disclosed a heart weighing over 400 gm., with slight hypertrophy of the left ventricular wall, which is consistent with a mild hypertensive heart. There was no infarction, and the coronary arteries were only slightly sclerotic. We found no real evidence of heart failure. There was about 50 cc. of fluid in both pleural

cavities. The liver showed no evidence of chronic passive congestion, but it was enlarged. In the region of the gall bladder was a mass about 6 or 8 cm. in diameter that completely replaced the gall bladder and that looked like carcinoma. It extended into the liver substance for about 4 or 5 cm. In cutting through this mass we found a gall-stone embedded within. Microscopic sections revealed that this was a primary carcinoma of the gall bladder. The increase in pulmonary markings was due to metastatic carcinoma.

Dr. Richardson: What about the bone marrow?

Dr. Castleman: There were also metastases to the peritoneum and to the bone marrow.

Dr. Schulz: Was the entire bone marrow replaced.

Dr. Castleman: We have not seen enough sections to say, but the one section that I examined certainly showed extensive involvement.

Dr. Jones: This woman was given sulfonamides with the idea that she had a bacterial pneumonia.

TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER, M.D.

Several materials have suddenly become available for the LYSIS OF NECROTIC TISSUES in empyema and other suppurating spaces. Streptokinase and streptodornase are being used on trial; they are obtained as fractions from cultures of a fungus. The enzyme Trypsin, produced by the pancreas, has also been found effective by Roettig and Curtis of Ohio State. . . . We have used the streptos on our first case of empyema. The signs of action (fever, pain, malaise) were brief and exactly as described. The fluid thinned and the evidence of necrosis decreased. The drug is said to have no effect on living tissue. . . . The perfect substance is probably in the future, but seems to be on the way.

More than a year ago this column contained the suggestion that Kendall and Hench would be good bets for a NOBEL PRIZE. . . . Because nobody else will remember that prediction, we now mention that they got it. . . . Minor point: the current Osler has no influence with the prize committee.

NEWS ABOUT NEWS SOURCES—A new medical journal will make its first appearance about now, January 1951. 'ANTIBIOTICS' will be published monthly by the Washington Institute of Medicine, with Dr. Henry Welch as editor, and all the leading authorities (fifty) as assistants,—Fleming, Waksman, Dubos, Finland, Keefer, Perrin Long, Woodward, Youmans, etc. . . . The AMERICAN JOURNAL OF NURSING has passed its fiftieth birthday, and should be read by every physician once a year, just for perspective. . . . The Health Information Foundation is potentially quite an outfit. It expects to work on unsolved diseases, improve the nation's health, collate and dispense information, and study such problems as health insurance. Officials from all of the leading drug manufacturing companies compose the membership. It also has potent sub-committees.

The Upjohn Company has A NEW PENICILLIN which can be used in cases where sensitivity develops to penicillin G. It is called 'Cer-O-Cillin', (or penicillin O), and the 'O' is derived from the smell, which is onion-like. . . . Oddly, when the

penicillin O has been given for a few days, it is said that penicillin G may again be used without a return of the allergic signs or symptoms. . . . Added note,—they have one type of penicillin, NOT on sale, which the lab calls 'penicillin S', for skunk.

Anaesthetists, hospital residents, and other experimenters, are enthusiastic about the NEW TINY PLASTIC TUBING (polyethylene) for intravenous and other uses. . . . For giving continuous fluids into a vein a tube may be fitted OVER a 19 gauge needle and INTO a 15 gauge needle. This combination is inserted into a little-used vessel, both needles are then withdrawn, and the tubing may be used and closed as desired. . . . It has also been used for intraspinal drugs, intraperitoneal drainage, and whatever else you can think of. It is flexible and transparent, and is most useful in children, irrational patients, the elderly, etc.

BOOKS-OF-THE-MONTH.—1. 'STRESS' by Dr. Hans Selye. . . . The book contains information on the currently important theory by which the adrenal responds to demands for function. . . . The stress sets off a reaction which produces 'desoxycortisone', which is the common cause of such ills as hypertension, rheumatoid arthritis, etc. . . . 'Strain' is the emotion which physicians will feel when they see the price of the book—\$14.00.

2. The numerous contributions of Tucson's W. Paul Holbrook and Donald E. Hill have been expanded to a 'MANUAL OF RHEUMATIC DISEASES'. It is a small book of 190 pages, with 119 illustrations, and is published by The Year Book Publishers, Inc., of Chicago. . . . The reviews are good, tho most of the comments so far are from the publisher and top-notch book-sellers. Year Book says "a practical, down-to-the-minute manual". Stacey's of San Francisco says, among other things "A concise, excellent presentation. . . . worthy of emulation in other medical fields."

Data are slow to gather and reach print on THE EFFECTS OF ADRENAL CORTICOID MATERIALS ON TUBERCULOSIS. The first brief reports were paradoxically clinical instead of experimental. . . . It is important to know the effects in order to answer several questions. Does cortisone or ACTH help tuberculosis? Does it aggravate tuberculosis if given for a real indication in the presence of clinical tuberculosis? Will it activate an inactive tuberculous lesion? . . . Dr. Emil Bogen, who visits this column at intervals, led a discussion on the subject at the Los Angeles Trudeau Society in late November. He used his animal inoculation work and a pair of cases to bring out other similarly small series from the audience. Correspondence from Philadelphia and other eastern sources was also mentioned. . . .

There are discrepancies and contradictions, but A FEW POINTS ARE NOTABLE,—(1) Symptoms of pulmonary tuberculosis are decreased, often greatly. (2) X-ray signs do not change, especially in chronic disease. (3) The hormones do not affect fibrosis which is already formed. (4) Tuberculin sensitivity may seem to be lost, but is probably decreased, and may vary during a series of several tests. (5) Streptomycin is effective during use of hormones, but less rather than more (as was hoped). (6) A worsening of the disease may follow discontinuance of the hormones, and certain species of animals may become more susceptible during usage. (7) Cortisone has no known effect on tubercle bacilli in vitro. (8) Therapy in silicosis would seem hazardous, because of a possible cryptic tuberculosis. (9) The effect of the hormones on animals inoculated with BCG is being studied. (10) Therapy of arthritis, etc., in the presence of tb., should proceed with caution, and only when necessary.

The **MODE OF CORTISONE ACTION** should become less secret soon. A radioactive form is now available for research. . . . Cortisone has been combined with tritium, a radioisotope of hydrogen. The drug was synthesized by Dr. T. Gallagher and colleagues at the Sloan-Kettering Institute in New York.

The Tumult over the importance of **VENOUS THROMBOSIS** persists, even tho the Shouting over the value of some of its therapy dies. . . . Such top-rank researchers and surgeons as Geza de Takats and Alton Ochsner are concerned over the frequency of thrombosis and its complications, while being disenchanted with anticoagulants and even proximal vein ligation. The latter is a chore; the former (especially dicoumarol) are hazardous; and both are not widely effective, they say. . . . Ochsner and Kay's use of alpha tocophoreol for thrombosis is aimed at increasing the blood anti-thrombin level, so that it may be in balance with prothrombin, so that clotting will not result. . . . We will have to wait and see.

RATS are still menaces to health and foes of medicine. Progress has been made in control efforts since the days of Zinsser's book about rats, lice, and fleas, but the balance is not much on our side. . . . Prof. Karl Link (who has several relatives in Tucson) has continued to invent drugs at the University of Wisconsin, and one of them may shift the balance against rodents. First it was 'Dicoumarol', now it is 'WARFARIN'. . . . The new drug has a similar formula, but it is nearly perfect as a rat poison. Rats will avoid drugs which they suspect to be death-dealing. 'Warfarin' does not cause suspicion, since it must be eaten repeatedly over a period of days, then causes drowsiness, ataxia, and death by internal hemorrhage, not near the source of food. . . . Humans and

pets are protected from over-dosage by the need for repeated ingestion and the size of the dose.

UNIVERSITY NEWS ITEMS.—The College of Pharmacy at the U. of A. has a new Dean. . . . The school was founded about two years ago by a retired Dean from Nebraska. He got the curriculum started, and now gives way to DR. HAAKON BANG. . . . Dr. Bang has been on the faculty at Washington State College since 1932, became a full professor in 1948. He obtained his first two degrees there in 1927 and 1931, and his Ph.D. from Purdue in 1942. . . . He also worked his way thru several commercial pharmacies in Washington, and is now becoming acquainted with the druggists of Arizona. . . . The 'West Coast Druggist' gives all these details, plus a picture.

BED-PANS have always seemed like too much of a chore for a sick-patient, not to mention an obstacle to defecation. . . . Unless the patient is handicapped by a cast or a paralysis or an acute unstable lesion it is easier and safer for him to use a commode or nearby toilet. . . . We have the evidence that most post-op. patients do better up; that many lesions, including most tuberculosis, heal just as well at modified bed-rest; and now the work of McGuire, which shows that the changes in intravascular pressure during use of a bed-pan are a hazard to the heart, the arteries, and the veins. A BAS the bedpan!

The third method for **TREATMENT OF ALCOHOLISM** which has appeared in the past year is now reported. . . . A type of myanesin called 'Tolserol' (mephanesin by Squibb) may be used for acute alcoholism, in either oral or intravenous doses. . . . It reduces abnormal neuromuscular impulses and has a sedative action without clouding consciousness. Ordinary sedatives may be cut down or out. . . . Side effects follow the I.V. approach, but the decrease in anxiety and jitters in a conscious patient may make it worthwhile.

HOUSE-DUST is somewhat of a mystery as well as a common cause of certain allergic conditions. It is even blamed for canker sores, abnormal fatigue, and other unexplained types of malaise. It is serious in winter, in children, and in areas other than Arizona. . . . The late Doctors Kibler and Watson of Tucson were noted for using house-dust extracts in the therapy of bronchitis. . . . Expensively decorated houses have often been stripped bare to accommodate an allergic member of the family. . . . Now we hear, from medical and non-medical sources, of a preparation called 'DUST-SEAL' which may be applied (without harm, it says here) to such dust-collecting items as furniture, carpeting, mattresses, bedding, curtains, etc. . . . The American Academy of Allergy has labelled it as 'a useful adjunct'. Time will

tell the true value (or perhaps it will be News-week).

CASE-FINDING by X-ray for tuberculosis, and for other diseases of the heart and lungs, has become 'SITUATIONAL'. . . . The method has long been used in colleges, and is used in an increasing number of medical and nursing schools, in offices and industries, in general hospitals, etc. It is urgently recommended now as a premarital examination—tho this lets it go until pretty late. . . . It is being used on a large scale in towns and cities, but this approach has notable flaws,—those in need of it often avoid it; those in the older age groups avoid it the most often. . . . We suggest here, for the first time, that if persuasion is needed for the olders, X-raying be tied up with something desirable. A written report that an x-ray had been taken could be required, for instance, **AT THE TIME OF PENSION APPLICATION.**

Sometimes Supply precedes the Demand. . . . Before most of us know much about **THE RELATIONSHIP OF LIPIDS AND LIPOPROTEINS TO ATHEROSCLEROSIS** (or before ANYONE knows much more), a laboratory in Belmont, California, offers to do the 'Gofman' test, on blood serum which can be sent to them. The concentration of **S 10-20** molecules is given in mgms % when the test is positive. . . . If one wishes to pioneer to this extent, it will cost \$30.00 per specimen.

1951 CANCER SYMPOSIUM

The Annual 1951 Cancer Symposium will be held in Salt Lake City, Utah., March 1 and 2.

Through the coordinated efforts of the cancer teaching group of the University of Utah—Medical School, and representatives of the Utah Chapter of the American Cancer Society, a two-day session has been arranged, each presentation being specifically designed to be of value to the practicing physician.

The Speakers: Dr. Buie from Mayo's, Dr. Huggins from Chicago, Dr. Garland from San Francisco, Dr. Bowers from Memphis, Dr. Ackerman from St. Louis, and Dr. Barnes from Columbus, have been carefully selected and are exceptionally qualified for this task. Formal talks will be held to a minimum and will be supplemented by a number of informal conferences, clinics, and seminars; and a televised operation by one of the visiting surgeons has been tentatively scheduled.

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CURB ON DOCTOR CHANGING?

Reprinted from Glasgow Scotland Bulletin

A curb may be put on the right of National Health Service patients in Scotland to change their doctors immediately as the result of an excessive number of changes.

Indicating this in its annual report, the Scottish Association of Executive Councils—whose annual conference will be held in Dumfries next week—says that amending regulations on the subject will probably be made in the near future by the Department of Health for Scotland.

The report says:—"It is suggested that a number of these changes are the result of a doctor conscientiously refusing to give a patient a medical certificate of incapacity or, it may be, refusing to issue a prescription for a medicament which the patient fancies."

While the association's executive committee

are anxious that the policy of free choice of a doctor should be preserved, it declares that a doctor should not be penalised for standing up to his conscientious opinion, especially when he was the man to judge whether the patient was fit for work or otherwise, and what was necessary for his proper treatment.

The new regulation proposed by the Department of Health, it is stated, will provide for immediate transfers in the case of patients removing from one district to another or where the doctors concerned consent.

But in other cases the patient will be allowed to transfer only after a fortnight's notice and after he has applied in writing to the executive council and has received permission to transfer.

A resolution to be submitted at the Dumfries conference will suggest that if the 14 days' notice method is adopted it should be only for an experimental period, and that if it fails the patient should be allowed to transfer at the end of a quarter, after giving a month's notice.

GREATER USE OF ANTICOAGULANT DRUGS URGED IN CUTTING HEART DEATHS

New "Clinical Progress" Section of "Circulation" reviews Treatment for Coronary Thrombosis

To help reduce deaths and disability resulting from heart disease, more general use of anti-coagulant drugs in the treatment of coronary thrombosis is recommended to physicians by Dr. Irving S. Wright, Professor of Clinical Medicine, Cornell University, New York City. Writing in the new "Clinical Progress" section of "Circulation," the Journal of the American Heart Association, Dr. Wright bases his recommendation on recent controlled experiments with heart patients. He suggests that other drugs recommended for therapy in coronary heart disease be subjected to similarly controlled studies before they are accepted by the medical profession as being of established value.

Dr. Wright's article, entitled "The Modern Treatment of Coronary Thrombosis with Myocardial Infarction," outlines the established therapy for this disorder, including rest, sedatives, alcohol, oxygen, and transfusions, as well as the administration of anticoagulant drugs.

The "Clinical Progress" section of "Circulation," in which the article appears, was inaugurated in the current (December) issue for the purpose of reviewing the latest advances in the

cardiovascular field as a guide to physicians. The editor of the new section is Dr. Herrman L. Blumgart, Professor of Medicine, Harvard Medical School.

Dr. Wright describes the use of the anticoagulants, heparin and dicumarol, and mentions the newer anticoagulant drug, tromexan, in the treatment of coronary thrombosis, a form of circulatory disorder that kills at least 200,000 people a year in the United States. He indicates that this figure will increase as the average age of the population continues to rise, thus presenting "a problem of increasing importance in national and community life."

Anticoagulants are used to check the spread of a blood clot, or thrombosis. Coronary thrombosis refers to the formation of a blood clot in one of the coronary arteries supplying the heart. The result of such a coronary thrombosis is the destruction of a part of the heart muscle. This is known to physicians as "myocardial infarction." The condition may be fatal or disabling.

Dr. Wright summarizes the results of a study by a committee of the American Heart Association in which teams in 16 leading hospitals in the United States observed in detail a total

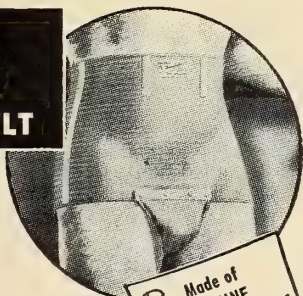
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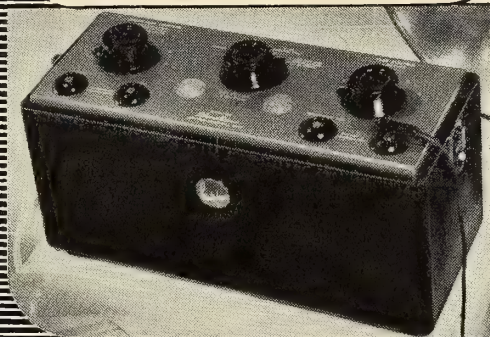
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of 1,031 cases that were submitted to careful statistical analysis. Approximately one-half of these received the best available type of treatment used prior to anticoagulant therapy. The other half received anticoagulant therapy in addition. Dr. Wright says the results were strongly in favor of the use of anticoagulants because of a marked reduction in the death rate and an even greater effect in preventing complications that leave patients with serious disabilities.

"On the other hand," Dr. Wright points out, "as is widely recognized, anticoagulant drugs are not without their hazards. They, like other forms of medical treatment, require skill and knowledge of the technique for their use. . . .

AMERICAN MEDICAL ASSOCIATION AIDS MEDICAL SCHOOLS

Cleveland, December 6—Responding to the challenge voiced by its president, Dr. Elmer L. Henderson of Louisville, Ky., in his address to the House of Delegates yesterday, that the medical profession take the initiative in raising private financing for hard-pressed medical schools, rather than seeking federal subsidies for medical education, the American Medical Association today appropriated a half million dollars as the nucleus of a fund to be raised for the aid of medical schools throughout the Nation.

The half million dollar contribution was voted unanimously by the A.M.A. Board of Trustees and was announced by its chairman, Dr. Louis H. Bauer of Hempstead, New York, at a dramatic, early morning meeting of the Association's House of Delegates today.

Dr. Bauer's statement follows:

"The Board of Trustees of the American Medical Association is pleased to announce to the House of Delegates that it has appropriated a half million dollars out of its National Education Campaign Fund, which was raised to defend medical freedom, for the aid and support of medical schools which are in need of additional financing.

"This fund will be given to the medical schools for their unrestricted use in their basic training of future physicians.

"This appropriation to aid the medical schools has been made possible by the widespread public cooperation which the profession has received from the American people in its campaign against Compulsory Health Insurance.

If anticoagulant therapy is employed with proper care the risks are not excessive.

Emphasizing the seriousness of coronary thrombosis, Dr. Wright says, "it occurs in all ages, but is predominantly encountered in persons over the age of 40. In general, it may be said that coronary thrombosis occurs at an average age which is approximately six years younger in men than in women. More men than women suffer and die from it in every age group under the age of 80. . . . One of the most unfortunate characteristics of this disease is that it strikes down many persons at the height of their productive years and activity, at times when they have the greatest responsibilities toward their communities and their families."

The fight against socialized medicine must go on until this issue has been clearly and finally resolved, but the pressure for regimentation of the medical profession has greatly lessened, due to the magnificent public support which we have received.

"The Board of Trustees, therefore, feels that it is keeping faith with the American people, who have given medicine such a splendid vote of confidence, when it contributes this amount to the medical schools of the National.

"There is growing public awareness that federal subsidy has come to be a burden, not a bounty, for it is bringing intolerable increases in taxation, and is dangerously increasing federal controls over our institutions and the lives of our people.

"American medicine feels very strongly that it should not seek federal aid for medical schools, until all other means of financing have been exhausted. The Board of Trustees announced yesterday its belief that funds for this purpose could be obtained from private sources—and as practical evidence of our sincerity of purpose, this appropriation has been made as the nucleus of a fund which we hope will be greatly augmented by contributions from many other sources.

"The Board hopes that this action will become a stimulus to other professions, industries, businesses, labor groups and private donors to contribute to this very important cause of protecting and advancing the interests of medical education and the public health.

(Continued on page 69)

"SOCIALIZED MEDICINE IS NO BARGAIN"

An address by William L. Hutcheson, General President, United Brotherhood of Carpenters and Joiners of America and Vice President of the American Federation of Labor.

Prepared for delivery at a Joint Session of the House of Delegates of the American Medical Association and the Third Annual Conference of the A.M.A. National Education Campaign, Cleveland, Ohio, Nationwide Broadcast, ABC Network, 4:00 p.m., December 7, 1950.

(Note: Mr. Hutcheson, due to illness, authorized the reading of his address to the Convention by his assistant, Mr. Peter E. Terzick, Editor of "The Carpenter.")

I am against socialized medicine. So is the organization which I have the honor of heading. At the Twenty-sixth General Convention of the United Brotherhood of Carpenters and Joiners of America, held in Cincinnati last September 1, 300 delegates, representing better than 54 per cent of the total membership, voted down a resolution to support the National Health Program. This probably does not jibe with the feelings of a good deal of the rest of the labor movement because much of the pressure for "free" medical care is coming from labor organizations. But it does reflect my sentiments and the sentiments of our recent convention.

Saving a dollar has never been distasteful to me. In fact I like to get as much for my money as the next man. That is one of the reasons why I oppose socialized medicine. It is no bargain. It looks cheap the way the backers present it, but when you dig down under the fancy layer of propaganda frosting you find that it can be mighty expensive. The British people have already discovered this fact. The July issue of International Labour Office, contains some very interesting data on the operation of the National Health Service in Britain. I quote a few lines of that report:

"The total (gross) cost of the National Health Service in 1948-1949, the first year of operation, greatly exceeded the original estimate. This was 265 million pounds, as against a revised estimate of 368 million pounds, with a net cost to the taxpayer of 278 million pounds. The revised estimate for the year 1949-1950 was 450 million pounds as against an original estimate of 352 million pounds. For the 1950-1951, the cost is estimated at 484 million pounds; in 1946 when the Bill was passed, the service was believed

to cost 167 million pounds a year."

In case you don't understand what the International Labour Office is, I can best explain its functions by quoting a bit from its preamble:

"The International Labour Office is an association of nations, financed by Governments and democratically controlled by representatives of Governments, of management and of Labour organizations.

"Its purpose is to promote social justice in all countries of the world. To this end it collects facts about labour and social conditions, formulates minimum international standards, and supervises their national application."

The I.L.O.'s publication, "International Labour Review," is published in the United Kingdom. As an international organization, I.L.O.'s findings are supposed to be strictly impartial.

Getting back to the report; if I read it correctly, service that was supposed to cost 167 pounds per year when the plan was set up in 1946 costs 484 million pounds per year, and the end is not yet in sight. By my old-fashioned kind of arithmetic that is an increase of better than 345 per cent and I am sure my poor old mother, who always made a dime do the work of a quarter, would not consider that kind of proposition any bargain.

I know! I know! The socialists claim that money is of no consequence in the matter of national health;—getting the poor the same quality and quantity of medical care as the rich can get under private enterprise is the advertised objective of the National Health Program. That sounds fine, too; but on Page 57 of the I.L.O. report, I find the following sentences:

"Survey of the distribution of doctors by boroughs shows that certain wealthier districts (of London) have an average of one doctor for 1,261 patients, while in the inner East End there are 2,472, or twice as many patients, per doctor. For a group of southern boroughs, the average is 2,897."

If that isn't the "one horse and one rabbit" recipe transferred from the meat pie maker's kitchen to the National Health program, then I need new reading glasses. I have tried to figure it from all angles but the answer I always come up with is that the lumbago, shingles and belly-aches of London's South Siders get only half the attention that similar ailments get in the swankier districts. For all the planning that has

been done, there is still an uneven distribution of doctors in London. If the backers of the National Health Program are to achieve their objective of equal health protection for all, the next step must be to tell doctors when and where and how they are to practice. Therein lies my greatest fear of socialization.

Socialization and death have one thing in common; you cannot be either a little bit socialized or a little bit dead. It is whole hog or nothing. After two years of the National Health Program, London doctors still have preferences as to where they want to practice. By compulsion of one kind or another, somebody is going to have to shoo doctors away from the fancy neighborhoods into the tenement districts or the program will wind up where it started. When the government is given authority to tell one group or one profession where and how its members are to work, no other group or profession can be safe for long.

If the day ever comes to America when Uncle Sam usurps the power to dictate to doctors under a health plan, it will be a sad day for carpenters. Adequate housing is still an unsolved problem in this country, especially for the poor. If it is logical to nationalize the medical profession to get more medical service for the poor, it is equally logical to nationalize the home construction industry to get roofs over the heads of the lower income groups.

I do not know much about doctors, but I know quite a bit about carpenters. They are an independent lot. They want to work where and how they please. The first bureaucrat who told a carpenter he had to work in Little Rock when he wanted to work in Lancaster would be gumming his food for lack of teeth. Carpenters want to be free agents; free to work where they want to; free to negotiate the terms of their wages and working conditions through collective bargaining; yes, even free to leave the industry and try their luck at something else if the spirit moves them.

They will retain these freedoms only so long as all other groups retain theirs. Socialization is like a wolf with a tapeworm; once it starts gnawing, it never can stop. Socialized medicine would only be the first bite out of our free enterprise system; it would not be many years before the carpenters would be feeling the teeth of socialization on the seats of their overalls. Any way you look at it, socialized medicine is

no bargain and the carpenters want none of it.

I know that the backers of the national health plan in this country resent the term "socialized medicine." They have all sorts of arguments to "prove" that doctors and patients will remain free as the air under their program. They make a strong case. Perhaps if human nature were less ornery and less avaricious, an idealistic health program might work out all right. But so long as people have preferences, so long as Park Avenue has more appeal than Hell's Kitchen, there will be an uneven distribution of doctors under any plan that does not contain compulsion. And once compulsion enters the picture, the rights and freedoms of all citizens stand in jeopardy. To me, it is as simple as that. For forty years, I have fought communism tooth and toenail because I do not want anyone pushing me around. I certainly do not want to put my head into a socialization noose voluntarily when the results can be as undesirable as communism.

I have always respected the medical profession for the fine contribution American medicine has made to human welfare. As I watched your battle against regimentation during the past two years, I have added to that respect. The physicians of this country have shown that they are willing to fight for their conviction. I salute you today not only as doctors but as crusading citizens as well. We in the labor movement have our own cross of regimentation to bear. The fight you are making is part of the same war. It is a war against concentration of authority in a few hands in Washington. As a veteran of forty years in the labor movement, I know what it is to fight for human rights. I am happy to take my stand beside you.

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BOOK REVIEWS

Santa Claus, M.D. By W. W. Bauer, M.D. Cloth \$2.75. Pp 266. The Bobbs-Merrill Company, Inc., Indianapolis—New York. 1950.

Bauer uses a popular style of writing to tell Johnnie Q. Public why the doctors of America favor Freedom in Medicine rather than compulsory health insurance. He de-bunks the phony statistics of the socialist propagandists. He points out clearly the progress in health matters that has come about under the traditional American manner of practicing medicine. He states the American way is best and has led to the highest health standards in the world. ("Swedes live longer in Minnesota than they do in Sweden.")

He (and we) are not, however, satisfied to stand still. More progress in health matters is our aim. Therefore Bauer discusses point by point, a chapter at a time, the twelve-point program of the American Medical Association for the improvement of health. He shows how this program in one point or another answers all the questions and criticisms offered by friend and foe alike. His are powerful arguments in favor of Freedom in Medicine and against compulsory health insurance.

The book is recommended reading for all doctors and their patients.

The Mask of Sanity: An Attempt to Clarify Some Issues About the So-called Psychopathic Personality. By Hervey Cleckley, M.D. Professor of Psychiatry and Neurology, University of Georgia Medical School, Augusta, Georgia. Second edition. Cloth. \$6.50. Pp 569. The C. V. Mosby Company, St. Louis, 1950.

Many detailed case histories are presented in this revised and enlarged second edition of Cleckley's book about the psychopathic personality. The voids, vacuums, and hiatuses in our knowledge of the subject are outstanding. New knowledge is needed concerning the classification, diagnosis, and treatment of the disorder. New types of institutions are required for the care of these patients. New laws must be formulated to enable the courts and doctors to protect these patients, their relatives, and the public.

Although much knowledge is left to be desired, progress is being made, and this book, with its presentation of known facts, its discussion of

future needs, and its philosophical approach to the problem, is outstandingly valuable.

The style of writing is designed for the non-medical reader as well as the doctor.

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already budgeted for this work during 1951.

"The Nation's medical schools are of the greatest importance to every American citizen and the A.M.A. has had the advancement of their standards as one of its main objectives for over 100 years. The Board of Trustees feels that if all other organizations and individuals will render support of this worthy cause in accordance with their financial ability that not only will the financial security of medical schools be assured, but that their freedom will be protected."

PERSONAL NOTES

The Maricopa County Medical Society held election of officers at its December meeting. *Dr. Leslie Smith*, Phoenix, was elected President-Elect; and will follow previously elected *Dr. Dermont W. Melick*, Phoenix, who will be President in 1951. *Dr. A. James Fillmore*, Mesa, was elected vice-president, and *Dr. Robert H. Cummings*, Phoenix, was elected Secretary-Treasurer.

Atomic Bomb Indoctrination was presented by *Drs. Donald Polson*, Phoenix, *Mark Westervelt*, Tempe, and *Seymour Fisher*, Phoenix, for the scientific portion of the December Maricopa County Medical Society meeting held at Good Samaritan Hospital Phoenix, December 4th. An excellent movie on medical care of atomic bomb casualties was presented.

The Arizona Heart Association has announced that beginning in January 1951 a clinic will be held at the Good Samaritan Hospital, for heart consultations for those people who could not otherwise afford cardiac consultation. Details will be divulged later.

Officers for the staff of the St. Joseph's Hospital, Phoenix, for 1951 were elected at the December 11th meeting. President is *Dr. Robert H. Stevens*, Vice-president, *Dr. Robert T. Phillips*, and Secretary *Dr. Donald A. Polson*, all of Phoenix. *Drs. Joseph M. Greer*, *Robert H. Cummings*, and *Robert G. Barfoot*, Phoenix, were elected to the executive committee.

An interesting symposium on Congenital Deformities was presented at the December 11th St. Joseph's Hospital Staff meeting. *Dr. Howard C. Lawrence*, Phoenix, spoke on "Congenital Deformities of the Foot," and *Dr. George A. Williamson*, Phoenix, on "Congenital Deformities of the Upper Extremity."

One of the finest medical papers in recent years was presented by *Dr. Leslie B. Smith*, Phoenix, before the staff of the Good Samaritan Hospital, November 27, 1950. It was on the subject of "Pericardial Effusion."

Officers of the Good Samaritan Hospital Staff for 1951 were elected at this meeting on November 27th. *Dr. Reed Shupe* was elected Chief of Staff, *Dr. Leslie B. Smith*, Vice-president, and *Dr. Donald B. Haislip*, Secretary. All are of Phoenix.

Dr. James J. Riordan, Phoenix, attended the Golden Jubilee of the American Roentgen Ray Society, St. Louis, Missouri, September 26-29th, 1950.

Dr. Robert L. Taylor, Phoenix, has left his position with the Veterans Administration Hospital, as Chief of Surgery at their Papago Park Hospital Phoenix, and has associated himself with *Dr. Karl Harris*, Phoenix in the practice of General Surgery.

The following doctors from the Maricopa County Medical Society have joined the armed forces: *Dr. Perry W. Bailey*, Phoenix and *Dr. Martin J. Kripke*, Mesa—the army. *Dr. R. A. Gutekurst*, formerly of the State Tuberculosis Sanatorium at Tempe, the Navy.

The November meeting of the Maricopa County Medical Society Scientific Session was addressed by three speakers. *Mr. Bob Bale* spoke on "Office Personnel Training" *Dr. Seymour Fisher*, Manager of the Veterans Administration Hospital, Papago Park on "Present Policies of the Veterans Administration" and *Mr. Grady Clark*, of St. Paul, Minnesota on "The Doctor and his Money (If Any) and his Future."

In Houston, Texas, November 7-10, 1950, the American Society of Anesthesiologists met. *Dr.*

Maxwell Palmer, Tucson, Drs. Audrey G. Urry, Wallace A. Reed and Geo. S. Enfield, of Phoenix were in attendance. Donald Snodgrass was also present. It seems the California delegation to this meeting was not solely trying to monopolize the water of the universe. If the meaning of this is obscure ask any of the above in attendance for explicit details.

The November meeting of St. Monica's Hospital, Phoenix, Arizona was held November 14, 1950. Drs. Howard C. Laurence, and John Rick-er, Phoenix, presented "Flap Repair of Lower Extremities," three case reports, and Dr. James M. Owens, Phoenix spoke and showed pictures on "Parlaryngectomy Combined with Cervical Esophagectomy in Cancer of these Regions."

St. Joseph's Hospital Phoenix, held its monthly staff conference November 10th. Dr. Joseph Ehrlich, Phoenix, correctly diagnosed a Clinico-

Pathologic Case as Perarteritis Nodosa. Further discussion of the case was given by Drs. Leslie R. Kober and O. O. Williams, Phoenix.

Dr. J. P. Ward, Phoenix, has been appointed director of the Welfare and Health Services, branch of Arizona's civilian defense program. October 23-27 in Washington, D. C. he attended the meeting of the association of State and Territorial Health Officers in his capacity of State Director of Public Health.

Dr. E. Payne Palmer, Sr., Phoenix, has been elected to the Board of Directors of the American College of Surgeons, at the Clinical Congress in Boston, Massachusetts.

Dr. Harry A. Cummings, Phoenix, attended the meeting of the American Academy of Dermatology and Syphilology in Chicago, Illinois, December 2nd to the 7th.

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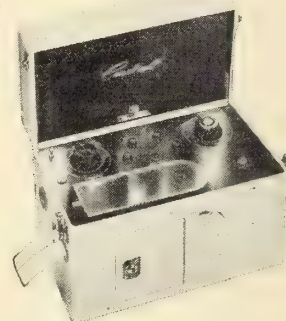
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SALINE SOLUTION IN TREATMENT OF BURN SHOCK*

The Surgery Study Section of the National Institutes of Health has recommended to the Surgeon General of the Public Health Service that the use of oral saline solutions be adopted as standard procedure in the treatment of shock due to burns and other injuries in the event of large-scale civilian catastrophe.

The recommendation followed action taken at the January 1950 meeting of the Surgery Study Section, when such treatment was approved in principle. Dr. Carl A. Moyer, a member of the Study Section, was designated at that time to prepare a memorandum suitable for submission to Dr. Norvin A. Kiefer, Director, Health Resources Division (now Health Resources Office), National Security Resources Board.

Dr. Moyer's memorandum, which was submitted to Dr. Kiefer, February 15, 1950, reads as follows:

"Since the publication of the experimental work of Dr. Rosenthal, Dr. Collier, et al., orally administered salt solutions have been employed in the treatment of burns at the University of Michigan Hospital, Ann Arbor, Mich.; at the Wayne County General Hospital, Eloise, Mich.; and at Parkland Hospital, Dallas, Tex. Personal clinical experience, in the above-named hospitals, has convinced me that the orally administered salt solutions are valuable adjunctive agents in the treatment of shock incident to burns, fractures, peritonitis, and acute anaphylactoid reactions. Certain factors are important in governing the effectiveness of the oral administration of salt solutions. They are as follows:

"1. The composition of the salt solution: The most palatable salt solution is made by dissolving 3 to 4 grams of sodium chloride and 2 to 3 grams of sodium citrate in each liter of water. If sodium citrate is not available, ordinary baking soda may be substituted for it.

"2. The concentration of salt should not be in excess of 140 milliequivalents of sodium per liter. If the concentration is above this, vomiting and diarrhea became important complicating factors.

"3. Whenever profound peripheral circulatory collapse is present, the intravenous route of administration must be used until peripheral blood

flow has been reestablished. The salt solutions that we have found most satisfactory for this purpose are Hartmann's solution (Lactate-Ringer's solution) or plasma. In addition to the salt solution or plasma intravenously, whole blood is given concurrently whenever peripheral circulatory collapse exists. This materially implements the effectiveness of salt solutions.

"The slightly hypotonic salt solution is the only drinking fluid permitted the injured individual until the edema of the injured parts begins to subside. Certain exceptions to this rule have to be made during the hot weather of summer when it is sometimes necessary to permit the partaking of some non-salty water.

"As much as 10 liters of the hypotonic salt solution have been drunk in the 24-hour period by adults who have been severely burned. Since salt solution has been substituted for water, as a drinkable fluid, no burned person who has lived for longer than 3 hours after being admitted to the hospital has suffered from anuria. The "early toxemia phase" of the burns has also failed to appear and the osmotic concentration of the plasma electrolytes has been well maintained.

"We feel that much more clinical observation and actual experimental work should be undertaken regarding the effectiveness of the basic principles of the supportive therapy of burns that have been so beautifully demonstrated by Dr. Rosenthal. It is obvious that the adoption of a more active program of investigation into the relative effectiveness of simple measures to combat shock would be of extreme importance to the Armed Forces and to the civilian population in the event of another war."

Because of the sharpened national emergency that developed during the summer of 1950, the Surgery Study Section, in approving Dr. Moyer's memorandum at its meeting on September 16, changed the last paragraph to read:

"While further clinical research concerning the effectiveness of oral salt solution in the treatment of burns and other injuries is certainly in order, there is already sufficient evidence to suggest that this form of treatment should be used in any large-scale disaster involving the civilian population."

The Surgery Study Section letter to the Surgeon General, dated September 16, 1950, reads as follows:

*From the Office of the Surgeon General, Washington 25, D. C.

"It is my understanding that one of the functions of the Study Sections is to offer advice to the Surgeon General in fields of medicine lying within the special competence of the Study Section members. At the January 1950 meeting of the Surgery Study Section, there was considerable discussion concerning the use of oral saline solutions in the treatment of burns and other serious injuries. It was the consensus of the Section at that time that, on the basis of the animal work which had been done by Dr. Rosenthal of the National Institutes of Health, and the clinical work which had been done by Dr. Carl A. Moyer, by the undersigned, and by others, the efficacy of such treatment had been definitely demonstrated and that, while there is need to stimulate additional research in this field, our present knowledge is sound enough so that action can be taken on this basis. Dr. Moyer was designated to draft a short memorandum expressing our point of view on this subject. Such a memorandum was prepared and furnished to Dr. Norvin C. Kiefer, Director, Health Resources Division, National Security Resources Board, on February 15, 1950. A copy of Dr. Moyer's memorandum is attached.

"In view of the more acute national emergency that has developed since Dr. Moyer wrote this memorandum, the Study Section, at its meeting on September 16, 1950, voted to recommend that the principles of treatment outlined in his memorandum be adopted for widespread use in any large-scale disaster involving the civilian population. Because of the present emergency situation, we have modified the last paragraph of Dr. Moyer's memorandum to read, 'While further clinical research concerning the effectiveness of oral salt solution in the treatment of burns and other injuries is certainly in order, there is already sufficient evidence to suggest that this form of treatment should be used in any large-scale disaster involving the civilian population.'

"You are at liberty to transmit this recommendation of the Surgery Study Section to the National Security Resources Board or to other proper agencies, and, if you see fit, to publish it. We feel strongly that it is important for the medical profession of the country and for those planning for the handling of potential disasters to be informed of the value of this simple and easily carried out form of treatment."

The letter was signed by Frederick A. Coller, M.D., University of Michigan, Chairman of the

Surgery Study Section. Members of the study section in addition to Dr. Coller, are: Dr. Claude S. Beck, professor of neuro-surgery, Western Reserve University; Dr. Loren R. Chandler, dean, Stanford University Medical School; Dr. Lester R. Dragstedt, professor of surgery, University of Chicago; Dr. Daniel C. Elkin, professor of surgery, Emory University; Dr. Carl A. Moyer, dean and professor of surgery, Southwestern Medical School, University of Texas; Dr. Harris B. Shumacker, Jr., professor of surgery, Indiana University Medical Center; Dr. Owen H. Wangenstein, professor of surgery, University of Minnesota; Dr. Allen O. Whipple, clinical director, Memorial Hospital, New York City; Dr. H. L. Skinner, chief of surgery, Staten Island Marine Hospital; Dr. Henry Beecher, professor of anesthesiology, Harvard University Medical School; Dr. J. Gordon Lee, chief of surgery, Mount Alto Hospital, Washington, D. C.; Dr. Howard R. Lawrence, chief of surgery, Francis E. Warren, Air Force Base Hospital, Wyoming; and Dr. G. Halsey Hunt, Chief, Division of Hospitals, Public Health Service.

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WOMAN'S AUXILIARY

1950 CONFERENCE REPORT

The report of Mrs. Royal W. Rudolph, President-elect, Woman's Auxiliary to the Arizona Medical Society, on the seventh annual conference of State Presidents and Presidents-elect, and National Chairmen of Standing Committees, at Hotel La Salle, Chicago, Illinois, November 2nd and 3rd.

Mrs. Arthur A. Herold, National President, graciously opened the conference with words of welcome and introduced the President-elect and Conference Chairman, Mrs. Harold F. Wahlquist. She, in turn, gave a plan of the meetings, presenting the overall theme, "Public Service Through Health Education"; the individual theme, "I Will Be Progressive."

Members of the National Board worked diligently to prepare for the conference and year's work. To give as much information as possible in two days, the "panel system" was used and it proved very successful. State presidents, assigned to the various standing committee panels, gave three-minute reports with the National Chairman acting as moderator of each committee. Speakers gave valuable and authoritative information in their specialized field. In order to pass on a vast amount of information, I have taken the liberty of condensing it into the following outline.

Organization—Mrs. Leo J. Schaefer, Chairman
"By your works ye shall be known"

1. Increase membership, unify efforts and stand ready to serve your community.
2. Invite new Auxiliaries to organize wherever county societies exist, no matter how few their members.
3. Enroll members-at-large. Whether an Auxiliary is or is not organized in a county, the individual doctor's wife is a key person in her community. She is urged to become a member-at-large in order to receive all benefits to pass on to her local organizations.
4. Retain members by planning active and constructive programs.

Program—Mrs. Harry F. Pohlmann, Chairman
"Flexibility necessary today"

- I. Program within the Auxiliary

1. School of instruction for state and county officers and committee chairmen. Summarize for county meetings.
2. Active public relations and alert legislative committees.
3. Welfare project.
4. Speakers' bureau.
5. Social gathering of doctors and wives.

II. Program outside the Auxiliary.

1. Health essay contest and debates in schools.
2. Educational movies and radio script programs.
3. A booth at county fair.
4. Rural health plans; Kansas has adopted a plan which has improved the distribution of doctors.

Public Relations—Mrs. Theodore E. Heinz, Chairman

"Live public relations"

I. Personal Education

1. County and state meetings.
2. Medical journals, *Woman's Auxiliary Bulletin*, *Arizona Medicine*, *Today's Health*, current magazines and newspapers.
3. Guidance and approval of your public relations activities from the Doctors' Advisory Council.

II. The Approach

1. Infiltrate various organizations, especially health agencies.
2. Establish friends in organizations and serve as liaison between the medical profession and lay people.

III. Activity Suggestions—Do you know 10,206 organizations have taken a stand against Compulsory Health Insurance?

1. Encourage women's clubs, such as A.A., U.W., League of Women Voters, P.T.A., P.E.O., and church groups to include the study of health plans on their agenda.
2. Work for endorsements. People are willing to take a stand when they understand the issue, but pushing causes antagonism. Endorsements should be urged only after there has been a program of orientation within the organization.

3. Recruit nurses. Many states are sponsoring the Nurses' Loan Fund. There is a need for nurses. We should recognize good nursing service and help them to maintain high standards. An annual tea for high school students, including freshmen, interested in the profession, has proved successful. Graduate nurses should be invited to speak on preparatory courses and explain the great service the nursing profession lends to humanity.
4. Explain and distribute literature on Compulsory and Voluntary Health Plans. Material is obtainable from county chairmen or from Miss Margaret Wolfe, 535 North Dearborn Street, Chicago.

Today's Health—"Most authentic health magazine"

- I. Mr. Frank Cargill, Circulating Manager
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 2. A magazine not for entertainment, but for instruction.
 3. Not a newsstand seller, but to be sold through personal approach.
 4. The larger the circulation, the better the magazine.
- II. Dr. W. W. Bauer, Publisher
 1. Appeal increased by change of name and cover.
 2. More money being paid to contributors.
 3. More articles written by nationally known people.
 4. Increased subscriptions due to variety of subjects of interest to all ages.
 5. Desire of staff for suggestions or constructive criticism.
- III. Mrs. W. Kelso, Chairman.
 1. Review an article at the county meetings.
 2. Urge doctors to subscribe 100%.
 3. Approach dentists, lawyers or other professional people.
 4. Sell or give subscriptions to the high schools and libraries.
 5. Be a subscriber yourself.

Legislation

- I. Mrs. Edgar E. Quayle, Chairman
 1. Discussing of pending bills by chairmen at the meetings has proved profitable.
 2. With approval of the Doctors' Advisory Committee, state and county chairmen

are urged to invite a well-qualified person to speak on legislative measures at the county meetings.

3. At the suggestion of the chairman, personal letters should be written to legislators by members and also by non-medical people.
- II. Mrs. Arthur A. Herold, National President, announced that the following resolution passed by the Auxiliary House of Delegates in San Francisco has been approved by the Doctors' Advisory Committee:

"Whereas, It is evident that existent trends toward socialism is governmental affairs call for a return to the fundamentals upon which this democracy was founded; and

Whereas, It has been brought to our attention that not all of the states in the Union require the study of American history from the first grade through the colleges; and

Whereas, Knowledge of the pledge of allegiance to the flag, the Declaration of Independence, and the Constitution of these United States creates in youth an awareness of our heritage of freedom; therefore be it

Resolved by the Woman's Auxiliary to the American Medical Association that our Advisory Council be petitioned to request that state auxiliaries stress within their respective communities the inclusion of the aforementioned subjects in school curricula."

- III. American nurses should know these facts about nurses in Great Britain:

"In November, 1941—five years before complete Nationalization of the health services—a Nurses' Salaries Committee with Lord Rushcliffe as chairman was set up. This committee consisting of two panels of equal numbers, one representing nurses, the other the employing authorities, made a survey. The Rushcliffe Committee made recommendations for increases in pay, a working period of a 96 hour fortnight and other badly needed improvements in the nursing field. By voluntary agreement these benefits went into effect throughout Great Britain generally in April, 1943.

To British nurses this improvement in their status represented a tremendous professional advance. And that step forward was accomplished by cooperation between the medical and nursing professions and lay people; *it was not the result of the National Health Service Act or any Governmental decree.*"

Dr. John Cline, President-elect, A.M.A.

"Don't be lulled into a state of stopping your work; effort of Auxiliary women has proved potent."

Dr. Ernest B. Howard, Assistant Secretary A.M.A. and liaison between A.M.A. and Auxiliary

- I. American College of Surgeons plan to continue the Hospitalization Standardization Program.
- II. A.M.A. studies and works constantly on legislation, health programs and draft act, informing doctors of progress.
- III. Auxiliary must keep informed; the next two years will be a crucial time in the fight against socialized medicine.

Dr. George M. Lyon, Special Assistant of Atomic Medicine and Chief Radio Isotope Section, Veterans Administration, Washington, D. C.

- I. Atomic Bomb. Oceans are no longer a barrier; in war, our cities will be targets with no complete defense.
 1. Greatest danger results from fire.
 2. Suffering and panic can be minimized.
- II. State Direction Civil Defense Program. Doctors' Advisory Committee is meeting a great challenge, initiating plans in the orientation of program.
 1. To educate the individual to educate himself.
 2. To prepare and plan with committees.
- III. Auxiliary Responsibility.
 1. Incorporate a study of civil defense into program.
 2. Stimulate other groups to study plans through lay group.
 3. Understand and interpret individual preparedness to communities.
- IV. Suggested Reading
 1. *How to Survive an Atomic Bomb*, by Dr. Richard Gerstell—25 cents. Bantam, Inc., 25 W. 45th St., New York City.
 2. *U. S. Civil Defense*—25 cents. U. S. Printing Office, Washington, D. C.

3. *Survival Under Atomic Attack*—10 cents. U. S. Printing Office, Washington, D. C.

Dr. Thomas G. Hull, Director, Bureau of Exhibits A.M.A.

"Health Education is an abstract subject; concrete by exhibits."

- I. Exposition type for outdoors.
- II. Table exhibits for county fair.
- III. Museum exhibits for those in receptive mind.

Mr. Ralph Greer, Bureau of Motion Pictures A.M.A.

- I. Local Procurement
 1. State Health Department
 2. U. of A.
 3. Cancer Society
 4. T. B. Association
 - II. A.M.A. Procurement. A limited number of scientific films are available for lay groups. The A.M.A. advises that a doctor should be present to discuss the films and that a question and answer period follow the showing.
 - III. Film Council of America, 57 E. Jackson Blvd., Chicago
 - IV. Television

A.M.A. is making survey to clear films.
- Whitaker and Baxter, Directors National Education Campaign.

Doctors are fighting for the health of the nation; they need the cooperation of every Auxiliary member. The medical profession is not fighting for personal gain today; it is fighting to preserve medical ideals in the future. America is a great country because the people have been unafraid; because of their love of freedom, they have made individual effort. Let us continue. Group endorsement is the result of individual endorsement. "Remember the powerful man in America today is the man next door."

In concluding this report I wish to say that I feel privileged to have been chosen to attend this splendid conference. The continuous working session gave everyone a gratifying sense of accomplishment. From the luncheons and regional breakfast, so thoughtfully planned, came the opportunity for a most rewarding exchange of ideas. And now, to you, let me repeat Mrs. Herold's last message, "Let us double our interest, triple our membership and quadruple our confidence."

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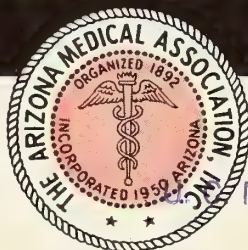
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Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 2



FEBRUARY, 1951

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(1) Mosenthal, H. O.: Management of Diabetes Mellitus: An Analysis of Present-Day Methods of Treatment, *Ann. Int. Med.*, 29:79 (July) 1948.

(2) McLester, J. S.: Nutrition and Diet in Health and Disease, 5th ed., Phil., W. B. Saunders Company, 1949, page 364.

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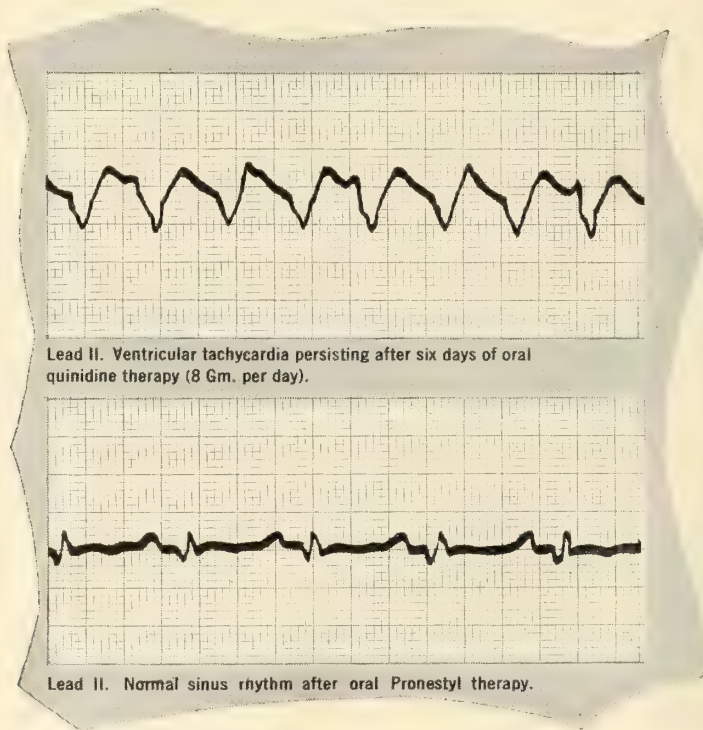


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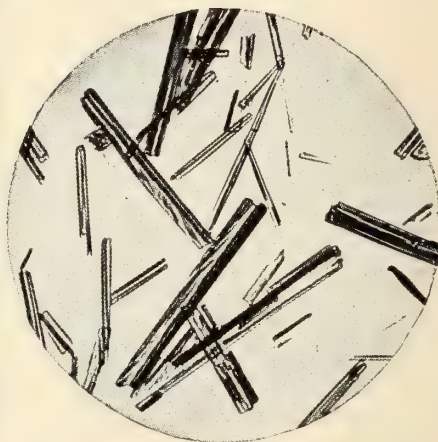
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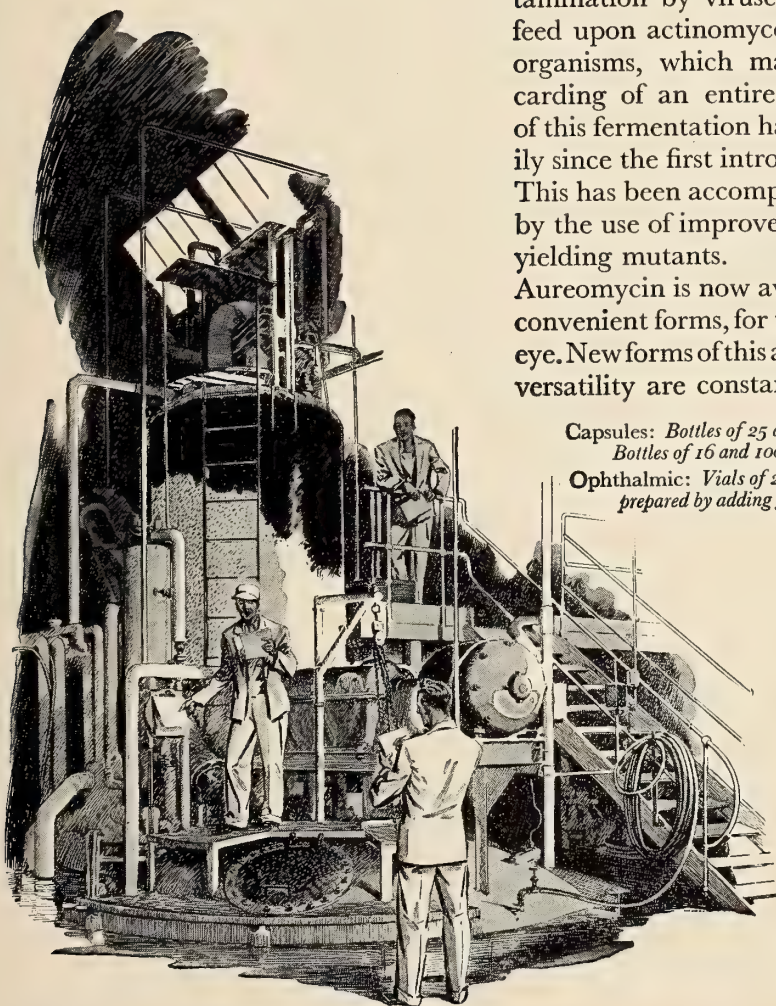
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1. LEHR, D. (1950), RELATIVE MERITS OF COMMONLY USED SULFONAMIDE DRUGS AS COMPONENTS OF MIXTURES, N. Y. STATE J. MED., 50:1361, JUNE.



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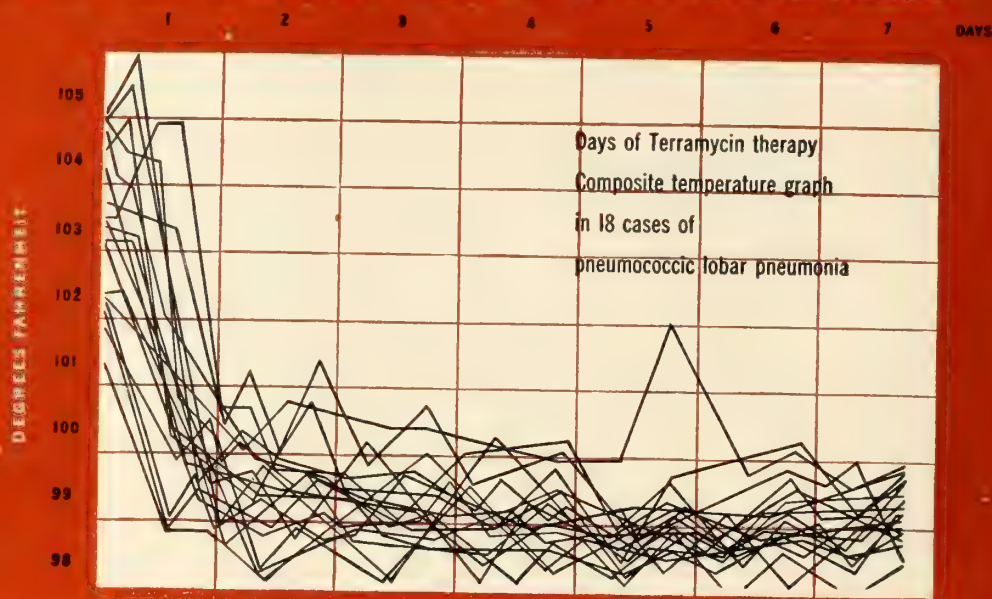
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1. Dennison, A.D.: *Jour. Med. Soc. New Jersey*, 46:139, Mar., 1949.

2. Saslaw, M.S.: *Jour. Florida Med. Assn.*, 34:657, May, 1948.

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1. Blake, C. F.; Friou, G. H., and Wagner, R. R.:
Yale J. Biol. and Med. 22:494 (July) 1950.

2. Herrell, W. E.; Heilman, F. R.; Wellman, W. E.,
and Bartholomew, L. A.: *Proc. Staff Meet. Mayo
Clin.* 25:183 (Apr. 12) 1950.

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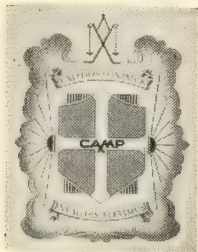
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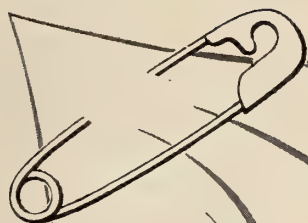
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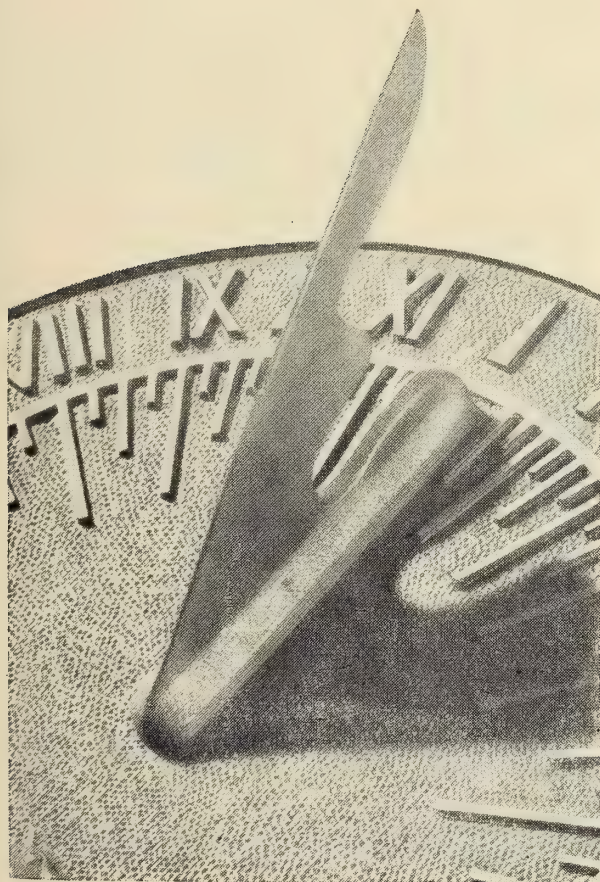


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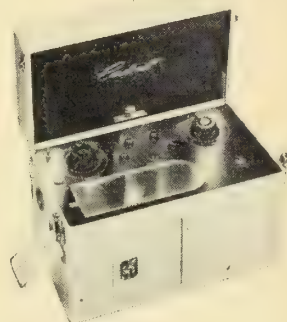
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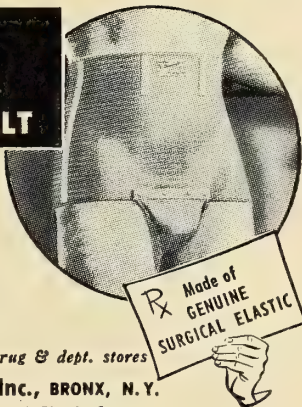
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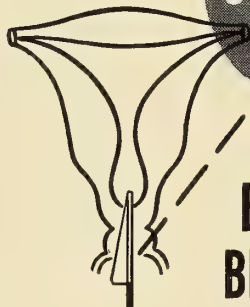
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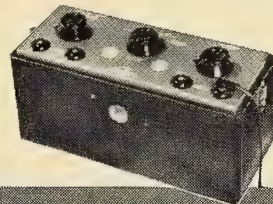


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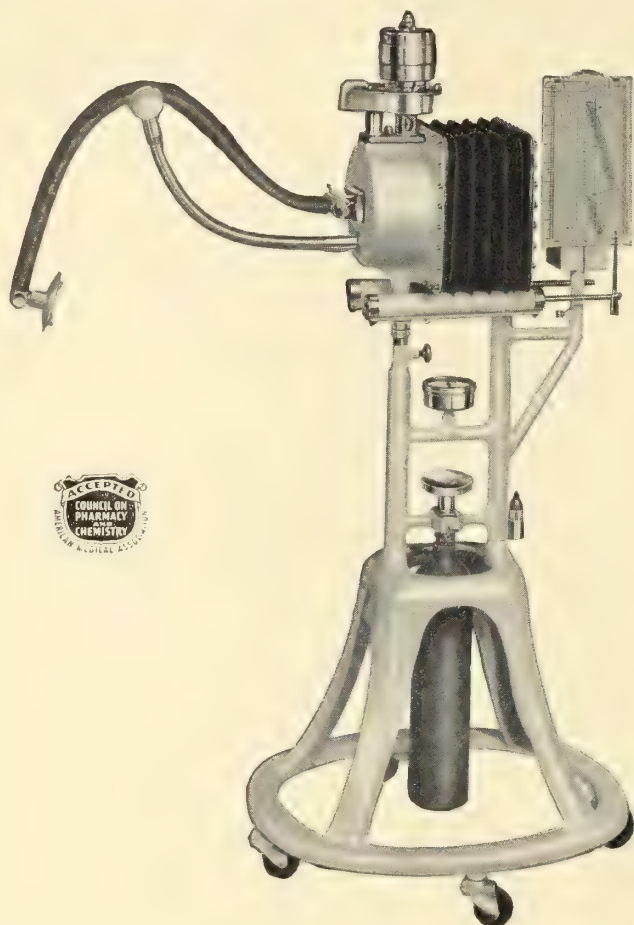
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VOL. 8, NO. 2



FEBRUARY, 1951

PLASTIC SURGERY FOR THE GENERAL SURGEON

W. R. MANNING, M.D., F.A.C.S.*

Tucson, Arizona

Plastic surgery might well be defined as being that specialty of surgery dealing with the restoration of defects both congenital or acquired which improve function and esthetic effect. It is therefore obvious, that there are a great many plastic surgical procedures used daily by the general surgeon as well as in other surgical specialties that might be termed plastic surgery. It becomes quite apropos that we discuss those principles of this particular field which might apply to general surgery, enabling us to do more for our patients.

One of the basic principles of plastic surgery is the interpretation of defects or disfigurements in terms of tissue loss, distortion and functional involvement. The preoperative planning of any surgical procedure should entail careful and thorough examination in order to estimate not only the loss of tissue but what tissues are involved as well as the degree of functional impairment. The general surgeon daily studies these problems in relation to practically any type procedures that he might carry out in regard to placement of incision, the approximation of tissue layers, the correction of distortion or tension.

Transplanted tissues should morphologically always resemble as close as possible the tissue which it is to replace. This applies to fascia, skin, mucous membrane etc. Skin transplants should be selected from an area which approximates the original as nearly as possible in regard to color, texture, thickness, as well as hair distribution. Another principle is that the repair of the defect must not produce another defect equally as great. This sounds as if it is a very simple and obviously understood principle,

and yet there are a great many attempts at repair which have resulted in disfigurement far greater than the original injury or defect.

A word should be said as to psychological considerations. There is no relationship existing between a person's physical defect and his reactions to it. Frequently we find patients with but a slight facial or bodily disfigurement who suffer a great deal more mental distress than those whose defects are severe and pronounced. Psychiatric consultation has been used and should be used more freely when a surgeon is confronted with a patient whose defect might be a reflection of a psychological state.

Besides the complete understanding of the patient's personality and his disfigurement or defect, one should make sure that the patient himself realizes the need for plastic surgical correction as well as the difficult and meticulous work that is to be required to correct such disfigurement. A patient who cooperates 100% makes the practice of surgery a pleasure. Photographic record should always be made both before and after operation and all views should be taken, particularly in color, in order to have a very definite and lasting impression in the file of the patient.

Preoperative Preparation

Preparation of the skin for operative procedures should utilize mechanical cleansing with soap and water and preferably 48 hours prior to surgery. The skin should not be stained by one of the colored antiseptics inasmuch that it removes the true color of epidermis as well as the faint lines that are so frequently used in the transposition of skin. Cyanosis is another factor that should not be masked and one of the clear antiseptics is preferable.

*American Board of Surgery. Read before Arizona State Medical Society, annual meeting, Phoenix, Arizona, May, 1950.

The preoperative preparation should pay careful attention to shaving of the skin so that such skin is not inadvertently nicked in the shaving process, and so that the exact position of all hair and point of hairline is noted and kept in mind by the surgeon. In working about the head, the eyebrows should NEVER be shaved. I have had occasion in the past two years to have seen three cases wherein the eyebrows were shaved by resident physicians in the hospital and to date these eyebrows have not returned. There remains in their place only a very short stubble which will take many years to grow to its normal length if it ever does produce normal hair length.

In immediate repair of lacerations nothing takes the place of thorough cleansing, copious lavage and careful debridement.

Instruments

While we seem to be talking about the field of plastic surgery as it is known as a specialty, we are actually speaking of the general surgeon who should be cognizant of simple plastic surgical principles, and the means to obtain equal results. In my opinion nothing can surpass fine instruments in this type of work. The skin can be handled freely providing one does not traumatize, which means that the mousetooth tissue forceps should be of a fine character, ordinarily one and two teeth. The G. B. New or the Adson pickups are admirable for this work.

Needles need not be many in character or type and two of the most generally acceptable are of an Anchor brand, one heavier for the buried catgut listed as an 1844-4, the other for the skin and listed as 1831-3. A very excellent adjunct in the help of handling skin is the use

of dural-hooks. When working about the face one should handle the skin as little as possible and these dural hooks serve admirably for positioning skin.

The knife blade should always be sharp and a new blade used quite frequently. It is absolutely essential that as straight and as right angle an incision as possible is made when going through skin. The number 15 blade is the most universally used.

Suture material should be as fine as a man can work with and depends entirely upon the area in which the work is being done. For the buried suture, it is my practice to utilize 4 or 5-0 catgut to approximate the fatty layer and utilize such catgut in the subcuticular layer which will slightly evert the skin edges and give coaptation without tension. Silk for the skin is my own personal preference although nylon, horsehair, cotton and steel are used by many men. In working about the face 5-0 and 6-0 depending upon the exact site of the approximation necessary are most commonly used. About the neck perhaps 4-0 is most universally used. Certainly nothing any larger than 4-0 should ever be used in any situation other than when the skin is extremely thick. If one desires to be exceptionally particular relative to coaptation, a subcuticular continuous steel wire threading from one side to the other as a pullout can be used although if the fine silk sutures are removed within 24-36 hours no stitch holes will ever remain.

The skin grafting instrument used depends upon ones own choice. My own preference, simply because I have used it the longest, is the Padgett-Hood Dermatome. I have had occasion to use the Reese Dermatome which carries with it the dermatape and is admirable for pattern grafts. Brown's electric knife is very excellent although I have had no personal experience with it, nor have I had with the Vacutome. Free handcutting with the Ferris-Smith, the Blair knife, are perfectly acceptable but again it is an individual variant as to proficiency of the operator.

Subcutaneous Closure

Prerequisite to any skin approximation is the closure or coaptation done beneath the skin level which is the most important part of any plastic surgical procedure directed toward the establishment of a fine scar. The fat layer should be obliterated by interrupted buried catgut,

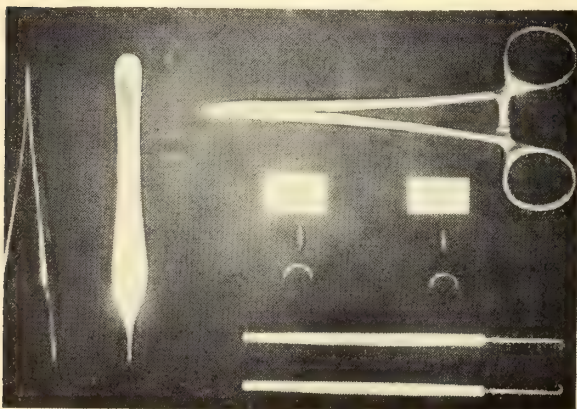


Fig. 1—Illustrating basic instruments essential in fine plastic technique—"pickups", needle holder, dural hooks and fine needles.

utilizing 4 or 5-0 or if one chooses the same size of cotton, silk or steel. The subcuticular stitches should be placed with an inverted type knot which is buried, utilizing very fine material, and allowing the skin to fall together.

The suture material in the epidermis itself is used only for very fine eversion and approximation and can all be removed within 24-36 hours. If a wound is approximated in its deeper layers with minimum and yet adequate amount of approximating material, the skin edges should require no tension whatsoever. The epidermis should have its cut edges slightly everted and there will be no necessity for bridging by fibrosis.

The skin suture should be placed closely together and on the face it is recommended that a suture be placed no further than $\frac{3}{16}$ of an inch apart having the knot on the side rather than across the wound edges. The sutures are placed so that there is no strangulation which can easily be identified by blanching at the point of entrance and exit of the suture material. It is helpful, I feel, particularly in wounds about the face, that no dressing be applied unless such is necessary from the standpoint of compression, as in skin grafting or with undermining.

The wound should be kept uncovered and the nurses instructed to free all serum from the wound particularly overlying the incision itself. Serum has a tendency to collect between the wound edges causing expansion and requires that approximation depends upon absorption of serum and replacement of fibrous material. Also, if the wound is kept clean from clotting or scabbing, there is less tendency for contamination than when sealed over by such excrement. The sutures are removed about the face— $\frac{1}{2}$ in 24

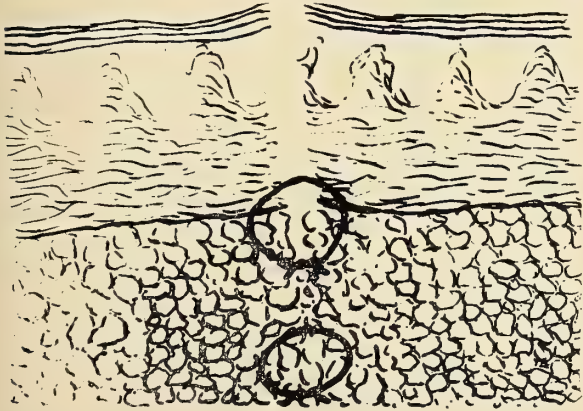


Fig. 2—Showing placement of subcutaneous inverted suture. Note inclusion of only minute amount of lowermost dermis. Relieves tension on skin suture.

hours—the remainder in 36, but with collodion or other bridging type dressing applied to continue support. If such incision is about the eyelids then closure and immobilization is effected by dressing to include not only the eyelid involved but both eyes.

SKIN SUTURE

- 1. INTERRUPTED
- 2. NOT OVER $\frac{3}{16}$ " APART

PLACEMENT



Produces further eversion and holds most tension on deeper layers

Knot on side

Fig. 3—Placement of skin suture. Note that the deep portion of suture holds most tension.



Fig. 4—Severe left temporal laceration at time of injury.

Langer's Lines

One of the most beneficial of all means we have of assuring ourselves of a minimal scar, is to place our incisions following Langer's lines. These lines have been carefully worked out



Fig. 5—Appearance at 24 hours. $\frac{1}{2}$ sutures removed at this time.



Fig. 6—Final appearance at 4 weeks. Scar hardly visible.

many years ago and have been confirmed in recent years by various authors. The theory is based upon the fact that the skin lines which are tension lines parallel the pull of the underlying muscles. Therefore, if one places the incision paralleling such tension lines, the pull will be along the line of incision rather than across it and will prevent retraction due to such muscle tension. There is one word of caution that should be observed and that is about the mouth and face the lines vary somewhat. It is very difficult to determine exactly how these skin lines vary although if one will ask the patient to purse the lips and show the teeth etc., going through all the various maneuvers of the facial musculature, one can see quite readily the lines that should be followed when an incision is to be placed on the face.

Skin Grafting

Grafting of skin is one of the most universal means we have of covering a defect whether it be traumatic or surgical. The skin, as we all know, can be cut to various thicknesses and anyone with a little patience and minimal amount of mechanical ability can adequately cut a skin graft to any thickness that he desires. The majority can easily use mechanical type of skin grafting instruments, namely the Dermatomes, rather than carry out difficult free hand cutting. There are many men in the country that can cut uniform free hand grafts with the knife, but I admit that I am certainly not one of them. The skin grafting procedure is most valuable when we think of coverage of such things as large traumatic defects, whether they be complete avulsion, burns, or any other type of epidermis removal. In the procedure of radical mastectomy when one must go extremely wide, the area can be very easily closed over utilizing a skin graft and allowing the patient to have a very satisfying result rather than all the trouble that follows with skin sutured under severe tension. Of course, in the treatment of burns, the use of the skin grafting is invaluable. A word should be mentioned to the fact that skin grafting should be done as early as possible, and not delayed beyond three to four weeks at the most.

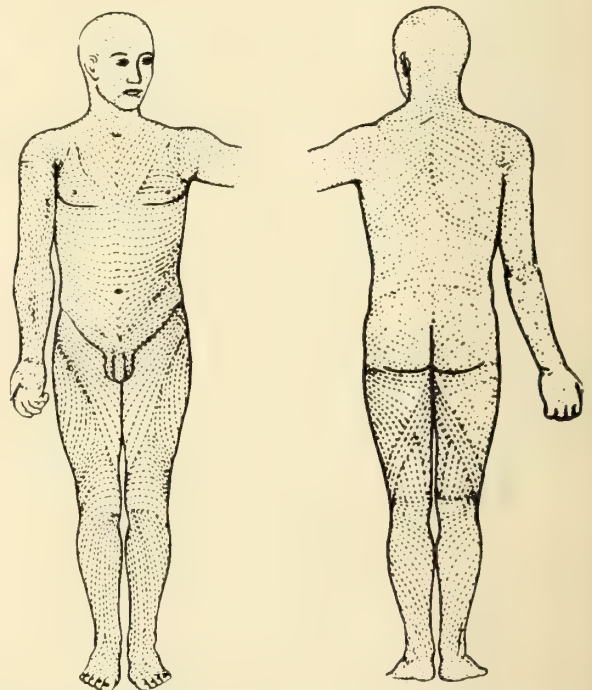


Fig. 7—Langer's lines—taken from Barsky "Plastic Surgery."

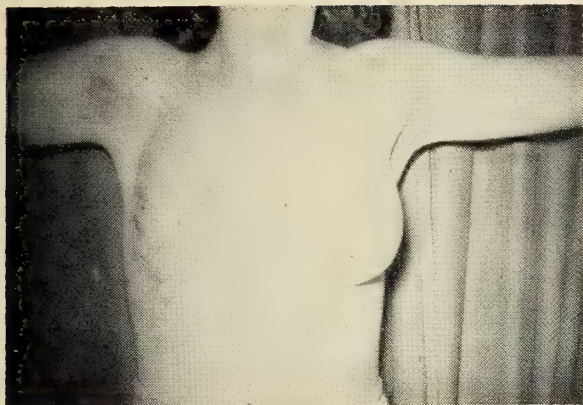


Fig. 8—Illustrating use of skin graft following wide radical mastectomy.



Fig. 9—Chronic leukemic ulcer of 4 years duration. Extremely painful.



Fig. 10—Ulcer grafted. Free of pain.

Still another use for our skin grafting procedure is the full or split thickness graft termed by many the "cutis graft", and used for severe recurrent type hernia. This graft is placed within the wound, obliterating all dead space and is sutured under definite tension. I have used this on several cases of hernial repair, when the patient had multiple episodes of recurrence, with very gratifying results.

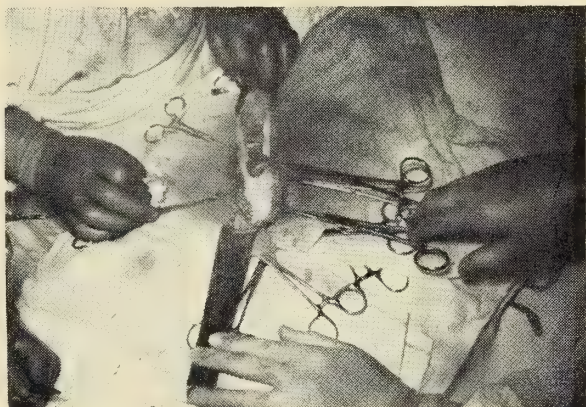


Fig. 11—Use of full thickness skin as buried graft in right inguinal herniorrhaphy.

Our postoperative treatment and follow up in grafting is of maximum importance because of the big and dangerous factor of infection. If we are grafting in an area where we are anticipating infection, such as about the buttocks or the perineum, it is my feeling that the wet technique of Kiskadden should be utilized. This technique embodies placement of the graft, coverage with two thickness of gauze and then laying of multiple catheters with heavy coverage over the entire dressing. The grafts are kept wet utilizing saline ordinarily, although if one anticipates or finds that the wound is contaminated with pyocyanous infection then dilute acetic acid can be alternated. This technique has produced remarkable results in areas which are infected or which are very prone to become infected.

I am going to mention pinch grafting only to condemn it. The pinch graft is a valuable procedure only when a small area is to be covered. The reasoning is sound for the fact that the donor site will be very disfigured from pinch grafting and the recipient area will not be left with a smooth, flexible covering, but it will be irregular, thick and disfiguring. As long as we have other means of grafting, certainly I feel we should utilize the pinch graft only in very small defects.

Z Plasty

The use of the Z plasty or the shifting flap technique is a procedure that is very old in regard to its origin but which has only been stressed relative to its importance, within recent years. It is a procedure that is quite simple but which is invaluable when one wishes to obtain skin length wherein there is shortening due to vertical scar, or contraction about the axilla, or such contractions as one sees in children with congenital bands about the extremities. This procedure can be done singly or it can be done in sequence. One obtains increase skin length with little difficulty. This procedure can be utilized with less difficulty in many instances where the skin, as it exists, is close to the range of normal and wherein we have been accustomed to replacement by graft. One has a tendency to forget this valuable means of irradiation of webbing and the elongation of skin area. I will illustrate some interesting stainless steel templates that are predetermined Z's utilizing the 60 degree angle and varying from 1/2 to 2 inches in length. These templates are certainly not original but are shown in the Journal of Plastic and Reconstructive Surgery. They make the use of the procedure quite simple even when one utilizes the small 1/2" Z at the corner of the eye and allows one to draw multiple Z's without worrying about the exact angles that are required.

Flaps — Tubes

Flaps can be single or double pedicle, either open or closed by grafting of raw exposed surface, or completely closed as a tube. These flaps and tubes can be transferred at one or multiple stages depending upon the quality and degree of supporting blood supply. The use of these procedures demands careful study of position, blood supply, transfer time, immobilization, skin character, etc. They are invaluable to cover the dorsum of a traumatized hand, exposed bone; add coverage and padding for partial amputation of a finger, cover large surgical defects of the face wherein lining (as in the mouth) is required. Again it is better to err on the side of conservatism and utilize multiple stage transfer than lose the entire tube or flap. For skin coverage where subcutaneous fat is needed this is the best and safest procedure.

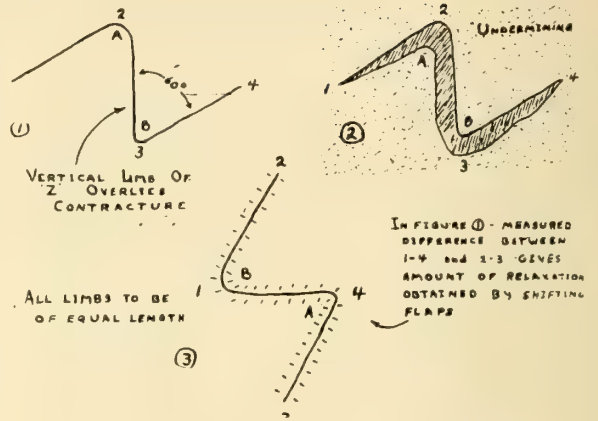


Fig. 12—Illustrates simple Z and reason why such procedure affords relaxation.

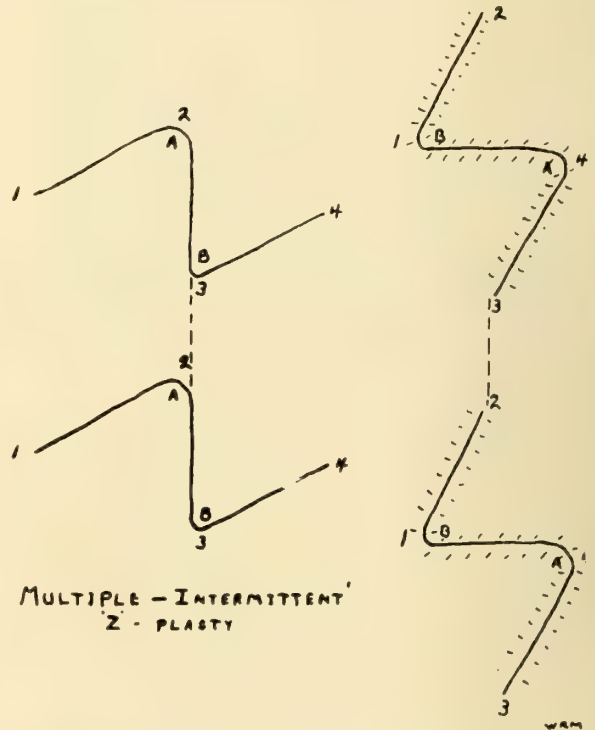


Fig. 13—Multiple intermittent Z plasty.

Summary

I have tried to point out a few of the basic principles of plastic surgery all of which can and should be utilized by the general surgeon. These principles are ones which all of us know but have a tendency to forget. If we will be painstaking enough to apply such principles, I am quite sure that the end results will in themselves gratify anyone for the time spent in application.

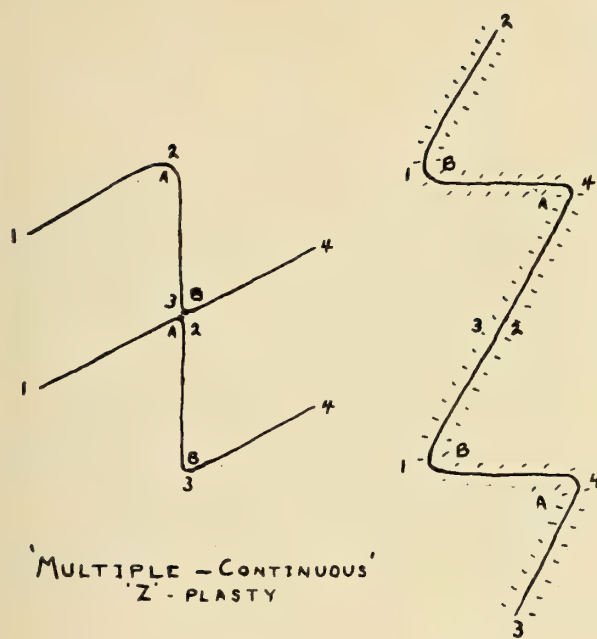


Fig. 14—Multiple continuous Z plasty. Can use any number of Z's.

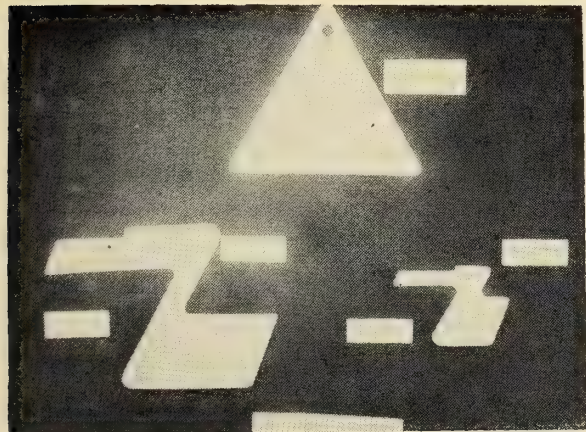


Fig. 15—Z templates made locally following article by Browne in Plastic and Reconstructive Surgery.

Remember basic principles:

1. The general surgeon can and should carry out plastic surgery techniques.
2. Preoperative planning is essential.
3. Have complete understanding with patient as to defect, need for correction, percent chance for good results, etc.
4. Photographs are invaluable.
5. Proper preoperative preparation
Attention to cleansing, shaving, debridement, etc.

Anesthesia—local or if general an understanding with anesthetist.

6. Instruments

Must be fine.

One cannot work on a watch with a plumbers wrench.

7. Postoperative attention to wound and particularly to graft may assure successful outcome of case.

8. Be meticulous and DON'T be in a hurry.

PEDICLE FLAP FOR FINGER-TIP



1. Abdominal skin incisions
2. Attachment to finger-tip
No raw surface exposed.

Fig. 16—Simple but valuable pedicle flap for partial amputation finger-tip.

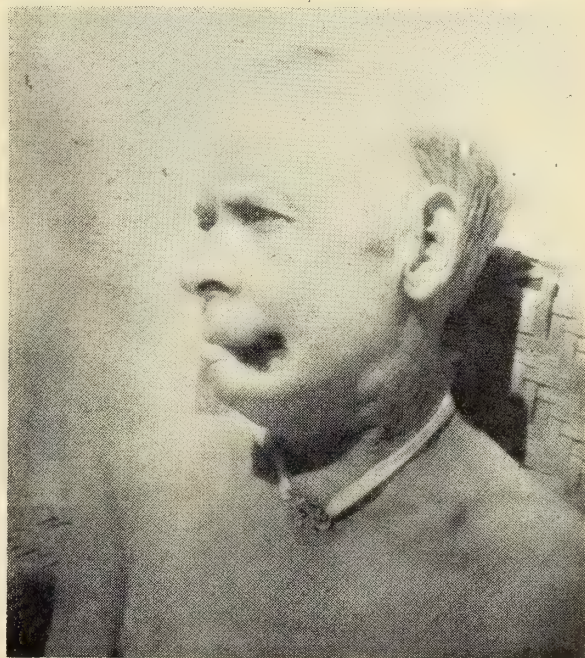


Fig. 17—Defect following surgery and x-ray therapy for malignancy lip and mandible.



Fig. 18—Long thoraco—abdominal tube formed to cover defect face.



Fig. 19—Defect closed. Final procedure to reform corner mouth needed.



STRANGULATED INGUINAL HERNIA

Study of 93 Cases

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INTRODUCTION

Intestinal obstruction has long ranked high among surgical emergencies. Strangulated external hernias constitute from 40 to 50 per cent of all of the cases of acute intestinal obstruction. These include, mainly, inguinal, femoral, ventral and epigastric hernias. The first two types are by far the most common and fortunately attended with a slightly lower mortality than ventral and epigastric strangulations. Simple uncomplicated inguinal hernia is perhaps one of the most frequent, if not the most frequent, correctable anomalies of the human body and standard methods of repair are known to every doctor. Yet this condition, when coupled with strangulated hernial contents, carries considerable risk to the life of the patient.

DEFINITIONS

The terms strangulation and incarceration were clarified for proper selection of cases and defined as follows: "Strangulated hernia—an irreducible hernia with clinical and pathologic evidence of circulatory disturbance of its contents. Circulatory changes may or may not be reversible." "Incarceration—an irreducible hernia without any clinical or pathologic evidence of circulatory disturbance. Mechanical obstruction may or may not be present."

MATERIALS AND METHODS

With these criteria as guides, a total of 93 cases of strangulated inguinal hernia were studied. The statistical results and observations in this paper are based on the clinical, surgical and pathologic findings in these 93 cases.

The surgical specimens represented in this series were examined both macroscopically and microscopically. Particular attention was given to the length of bowel involved, the character of the distal and proximal portions and the mesentery of the bowel. An effort was made to correlate these findings with the clinical signs and symptoms as an aid to diagnosis and pathology present. Where applicable, comparisons have been made with similar studies found in the literature.

HISTORY

Strangulated hernia has a history dating back to 3000 B.C. when an Egyptian priest initiated the belief that it was due to fecal impactions. It was not until the 17th century that this theory was disproved. The names of men famous in ancient medical science, as Roger of Salerano, Vesalius, Fallopius, Scarpa and many others all were prominent leaders. It may be said that the progress of treatment of this condition in general paralleled understanding of the anatomy, pathologica, and physiology involved.

PATHOLOGIC PHYSIOLOGY

It has been shown that inguinal herniations most commonly pass through one or more of three elastic openings in the anterior abdominal wall. The hernial contents are contained in a peritoneal sac and consists in the main of small intestine or omental fat. The elasticity of these anatomical structures render strangulation of the contents relatively less frequent than when rigid structures are encountered, as for instance with the femoral hernia. An increase in the intraabdominal pressure forces the hernia content through these elastic rings. If intestine is contained, gas and fluid bowel content are included. Continued peristalsis continues to fill the loop with gas or fluid material. Should the pressure persist for a short time, the elastic ring may compress the venous component of the mesenteric circulation, initiating circulatory embarrassment of the hernia contents. Continued arterial pulsation adds to the venous stasis and soon all the blood vessels and capillaries are "stuffed" with red blood cells. The picture of venous congestion, edema and swelling of the bowel wall rapidly follows until the pressure at the site of the constriction equals the arterial pressure and closes the lumen of the contained bowel, in effect, forming a closed loop obstruction with the mesenteric vessels occluded.

Transudation of fluid into the bowel wall, lumen and hernial sac soon ensues. The degree of fluid is largely determined by the length of bowel segment involved and whether the venous obstruction predominates. This latter showed

the greatest blood loss in experiments conducted by Wangenstein. An average of 59 per cent blood loss occurred in this group as compared to 35 per cent when arteries, veins and bowel were ligated. There was no fluid loss with pure arterial ligation. Early the transudated fluid is clear but progresses to serosanguineous color. This blood plasma loss may be enough to produce the picture of surgical shock.

The strangulated contents become increasingly gangrenous as the pathologic process proceeds. With decreased bowel viability the wall permeability increases. Passage of bacteria into the peritoneal cavity results. Positive cultures of streptococcus hemolyticus, bacillus coli, staphylococcus, bacillus aerogenes and numerous others may be obtained from the peritoneal fluid at this gangrenous stage. Bacteria may occasionally be demonstrated when the fluid is clear.

FREQUENCY

Strangulation occurred in approximately 1 per cent of all inguinal hernias and constituted about 1.7 per cent of all surgical emergencies of the abdomen and pelvis. Together with other external hernias it accounted for 53 per cent of all the causes of acute intestinal obstruction.

AGE AND SEX INCIDENCE WITH THE SITE OF HERNIA

This disease is predominantly a problem of geriatrics, the greatest incidence occurring between the 5th to the 8th decades with the peak between 60 and 70 years of age. The average for the series was 51.2 years. 90.3 per cent of the cases were found in males, with the ratio of right to left side of 2.2 to 1.0. Those patients below 10 years, the incidence of males to females was 11 to 1 and the right to left side 10 to 2. The mortality rate of 93 cases was 14.0 per cent.

OTHER PREDISPOSING FACTORS

Other predisposing factors of questionable value were occupation and social status. A history of the direct inciting cause of the strangulation was apparent in only about 10 per cent and included lifting heavy objects and upper respiratory infections, mainly.

SITE OF STRANGULATION

In order of frequency, the neck of the sac, the external, and internal rings were found to be the mechanical agent responsible for the strangulation. The last named was attended with the highest mortality rate.

DURATION OF SIMPLE HERNIA AND TRUSS

It was deduced from the statistics that the length of time that the patient has a hernia bares no particular relationship to the incidence of strangulation. It may occur early as it did in 9 cases or later after a lapse of 30 to 40 years. 29 of the patients gave a history of wearing a truss for varying lengths of time. There was one death in this group and 7 resections of the strangulated contents, including one of small intestine. A constant pressure, such as a pad would exert could very easily produce a chronic inflammatory process with result of scarring of the underlying tissue, perhaps adding to the fibrosis or constriction of the neck of the hernia sac. This has been cited as an etiological agent in strangulation.

TAXIS

No cases of reduction "en bloc" occurred in this group; however 28 per cent of the patients had attempted taxis of varying degrees of gentleness and skill. Other forms of cure were hot packs, cold packs, enemas, laxatives, anaesthetics and various combinations of these.

McLaurin, an Australian surgeon, summed up the subject of taxis effectively as early as 1920: "I have no hesitation in saying that is safer to do an early operation, even by candle light in a "bush-humpy" without a nurse and by local anaesthesia than to venture upon the perilous seas of taxis."

CLINICAL MANIFESTATIONS

The diagnosis of strangulated inguinal hernia was no problem in this series, being correct in 96.8 per cent. The symptoms and signs were those of an acute abdomen with evidence of intestinal obstruction and the presence of a painful hernial mass. It was indicated that differentiating strangulated omentum from intestine, clinically could be made with a fair degree of accuracy by the significantly low percentage of occurrence of absence of colicky abdominal pain, fecal vomiting, obstipation, rigidity, distention or visible peristalsis in the omental group. The degree of strangulation present in the intestinal group was impossible to tell with any certainty because of the overlap of clinical manifestation. The temperature, pulse and white count, urinalysis and blood chemistries were not of particular diagnostic aid except as to the general condition of the patient.

It may be said that all of these were elevated when definitely gangrenous hernia sac contents are present, usually the highest being found with gangrenous intestine. X-ray aid was sought only in a very small number of cases and was 100 per cent correct for intestinal obstruction.

DURATION OF SYMPTOMS

Although the duration of symptoms had a direct bearing on the general condition of the patient, it was indicated that the severity of the constricting mechanism was more fundamentally concerned with the mortality rates. Also the time element seemed to be of little importance when tissue *other* than bowel was involved.

PREPARATION OF PATIENT FOR SURGERY

Preparation of the patient for surgery should be concerned with the aggressive restoration of the water and electrolyte balance, the correction of the blood volume and the elevation of the blood pressure if there is clinical evidence of shock. Also if gangrenous or perforated bowel is suspected, chemotherapeutic or antibiotic agents instituted. A planned procedure for replacing body proteins should be formulated if there is evidence of malnutrition or that the plasma proteins are low. Intubation as a sole remedial agent in the treatment of strangulated obstruction is to be condemned but when used as an adjunct prior to or during surgery as a means of emptying the stomach contents, is a valuable aid.

CONTENTS OF SAC

78.5 per cent of the 93 cases had small intestine strangulated in the hernial sac. The large intestine was involved in only 2 cases, neither of which resulted fatally. Of special interest was one case in which the hernial sac contained bloody fluid but the contents slipped back into the abdomen before visualized by the surgeon and no attempt was made to search for the involved tissue. Fortunately this patient lived.

TYPES OF HERNIA

Types of hernias found were not remarkable, 84 per cent being indirect inguinal. Direct inguinal, sliding and Richter's type made up the remainder.

BOWEL VIABILITY

Corollation of the character of the abdominal

fluid, the appearance of the bowel and the mesentery with bowel viability was indecisive. No criteria could be determined with which to judge questionable areas. Generally it was found that the presence of free bloody fluid indicated bowel damage; however if not present, it did not exclude strangulation. The dynamics of bowel color and motility were infinitely more important in the questionable cases than the static qualities, that is, a visual improvement in the circulation indicated patency of the blood vessels. These were enhanced by inhalations of 100 per cent oxygen and warming with moist saline compresses. Pulsation of the mesenteric vessels was noteworthy and necessary to determine viability. Edema of the mesentery seemed to make little difference. Specific tests for viability were not used on any of the 93 cases other than the 100 per cent oxygen. The fluorescein and procaine hydrochloride tests are worthy of consideration.

OPERATIVE PROCEDURES

The group in which bowel was involved but reduced as being viable had a mortality rate of 0.6 per cent as compared to 53.8 per cent mortality where it was judged gangrenous and a definitive procedure instituted. The results of the latter were very striking. All those in which some temporizing procedure was done (enterostomy, exteriorization or ileostomy) terminated fatally. All those, in which a resection was done lived. There was no fatality in the two cases requiring a folding suture (Sumner type) repair of a portion of the bowel wall.

There were no cases in this series to demonstrate the efficacy of removal of the gangrenous bowel enclosed within an unopened hernial sac nor of an aseptic bowel anastomosis. The recent literature indicates these procedures, together with primary resection of strangulated intestine, would perhaps aid in lowering mortality in strangulated inguinal hernias.

The types of hernial repair following relief of the strangulation obstruction varied considerably. The Andrews-Bassini being the most popular. No repair was done in 7 of the 93 cases because of the general condition of the patient.

COMPLICATIONS

Most common complications resulting fatally were peritonitis, toxemia and shock. There were only two fatalities from pneumonia.

PATHOLOGY

Pathologic observations were made from the macroscopic and microscopic study of the surgically removed specimens. All tissues examined showed gross and microscopic evidence of blood congestion, edema and hemorrhagic infarction. Disintegration was apparent in the advanced examples of gangrene.

CONCLUSIONS

In conclusion it might be stated that:

(1) Strangulation of an inguinal hernia comprises a considerable group of surgical emergencies in which the mortality rate has remained persistently high.

(2) The mortality rate in uncomplicated inguinal hernias is exceedingly low.

(3) The constricting agent in strangulation has been shown to be a fibrous ring in the neck of the sac, the external and internal ring. That more strangulations do not occur in this type hernia is due to the absence of any rigid structures.

(4) Strangulated inguinal hernia is seen predominately in males between the sixth and seventh decades and usually on the right side.

(5) Duration of the hernia does not affect the mortality rate.

(6) Previous herniotomy or wearing of a truss does not affect mortality.

(7) Associated medical conditions had no bearing on the strangulations, but affected the mortality indirectly through the general condition of the patient.

(8) Taxis for strangulated or incarcerated inguinal hernia is to be condemned because of the possibility of reduction en bloc or reduction of non-viable bowel.

(9) The correct diagnosis of strangulated inguinal hernia was made in 96.8 per cent of the cases.

(10) The clinical differentiation between strangulated intestine and omentum in the hernia sac of a strangulated hernia may be made with a fair degree of accuracy.

(11) The degree of strangulation of bowel present is impossible to determine clinically with any degree of certainty.

(12) The duration of symptoms are of secondary importance; the severity of the constricting mechanism is a fundamental factor in determining the prognosis of bowel viability.

(13) Aggressive replacement of water and electrolyte losses, correction of blood volume and the blood pressure with whole blood and plasma, and instituting chemotherapy is strongly indicated in the preparation of the patient for surgery.

(14) Strangulated contents exclusive of intestine do not affect the mortality rate in strangulated inguinal hernia.

(15) Determination of bowel viability is very difficult in questionable cases of strangulated inguinal hernia.

(16) The mortality rate is high when the strangulated intestine is definitely gangrenous.

(17) Enterostomy, exteriorization or combination of those is considered an unsafe surgical procedure attended with a very high mortality rate when used on patients with gangrenous bowel.

(18) Primary resection of the involved bowel is the surgical procedure of choice—with amputation of the gangrenous loop.

(19) The removal of gangrenous bowel within an unopened hernia sac should be considered in strangulated inguinal hernia.

(20) Aseptic, oblique, end-to-end anastomosis should be considered as a procedure in lessening peritoneal contamination and overcoming the difficulties of anastomosing distended to collapsed bowel.

(21) The early use of massive doses of penicillin or penicillin with streptomycin, the aggressive replacement of electrolytes, the control of shock and loss of proteins by whole blood or plasma and the resection of gangrenous bowel are considered the main factors in lowering the mortality rate in strangulated inguinal hernia.



PULMONARY DENERVATION FOR INTRACTABLE BRONCHIAL ASTHMA*

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INTRODUCTION

This subject is presented as a preliminary, objective and factual report of sixteen operations on twelve patients for the relief of intractable bronchial asthma. Insufficient time has elapsed to warrant either an appraisal or a condemnation of the procedure. Only those patients with intrinsic, intractable bronchial asthma of long duration with no relief from medication were considered as possible candidates. Bronchoscopy and bilateral bronchography were deemed necessary in ruling out other causes of bronchial wheeze. It was recognized that there are two broad clinical types of asthma. The first type includes those cases with a definite allergenic sensitivity with mucosal edema, congestion and increased secretion. They are usually seasonal and relieved by the antihistaminic drugs or desensitization. The second type comprises those patients with no distinct allergy but with recurrent infection in some portion of the respiratory tract. Here the bronchospasm involves reflexes originating in the bronchi. Denervation operations were done only on patients of the second type.

Most of the patients were given prolonged deep ether anesthesia and bronchoscopy for temporary relief from the intractable status. If such relief was not obtained, operation was deemed inadvisable.

PHYSIOLOGY

The physiologic basis for surgical treatment of intractable asthma is based upon the following facts:

- (1) The bronchiole, with an absence of cartilage and a relative increase of smooth muscle, is the principal site of spasm.
- (2) The vagus is the afferent pathway to the posterior pulmonary plexus.
- (3) The sympathetic chain is the efferent pathway from the posterior pulmonary plexus.
- (4) Stimulation of the distal end of the cut vagus causes bronchoconstriction. After nerve degeneration or atropinization bronchoconstriction is absent.

(5) Stimulation of the peripheral end of the cut sympathetic causes bronchodilation.

(6) Vagal and sympathetic fibers have homolateral and contralateral innervation.

(7) The posterior pulmonary plexus, the principal source of innervation of the lung, receives nerve fibers via the bronchus, the sheath of the pulmonary artery, and probably other root structures.

HISTORICAL

Kummel of Germany, in 1923, first did a cervical sympathectomy for the relief of intractable asthma and reported several cases of apparent cure. In 1924, Kappis reported 100 cases of right vagotomy with varying degrees of success. In 1926, Kummel reported his experience with section of the posterior pulmonary plexus. Also in 1926, Leriche of France recounted his experience with ramisection of the first four thoracic rami communicantes. In 1938, Reinhoff reported eleven cases of bilateral resection of vagal branches to the posterior pulmonary plexus. In 1942, Reinhoff and Gay reported twenty-one cases in whom a similar procedure was used; of these, seven were successful, although nine cases died within the first seven days following operation. In 1948, Dr. Brian Blades, in a personal communication in which he described the operative technique for the more thorough interruption of the pulmonary innervation, wrote: "Some dramatic results—some failures. Another year before we can be certain about final results."

SURGICAL TECHNIQUE

The surgical technique followed here is as follows: Right lung denervation is done first. A postero-lateral segment of the sixth rib is resected and the thoracic cage entered. The azygos vein is doubly ligated, transected and transected. The vagus nerve is exposed and all rami going to the bronchus and the posterior pulmonary plexus are doubly ligated and transected (below the recurrent laryngeal). The plexus around the main bronchus is destroyed and the sheath of the pulmonary artery is destroyed. At closure two water seal tubes are used and rapid expansion of the lung obtained. Left denervation is done several months later, if needed.

*Actually the word "denervation" is not a satisfactory term. It is used here in the absence of a more truly descriptive terminology and for the sake of brevity.

**Read before the 1949 meeting, Arizona Trudeau Society

Case No.	Sex	Age	Dur. of Asthma	Resid. in Ariz.	Date of first Observ.	Vit. Cap. before Aer. Insp.	Vit. Cap. after Aer. Insp.	Deep ether Anesth. and Bronch.	R. Pul. Denerv.	L. Pul. Denerv.	Present Status (May 1950)	Comment
1.	Fe	63	17 yrs.	2 yrs.	10/2/47	50%	70%	7/27/49 relief 1 mo. 11/30/48 11/17/49			no asthma	
2.	Fe	60	20 yrs.	1 yr.	1/15/49	46%	66%	2/17/49	2/23/49		Mild wheeze 2 mm adren. relieves	
3.	M	40	9 yrs.	1 yr.	1/26/49	40%	76%	1/29 4/28 7/1 - 10/4	3/1/49	10/17/49	no asthma	
4.	M	50	18 yrs.	1 yr.	2/15/49	22%	63%		3/19/49		4/28/49 mild asthma	overdose of Demerol. Expired
5.	Fe	26	5 yrs.	1 yr.	2/5/49	36%	73%	3/15/49 9/11/49	5/26/49		Some degree of asthma	
6.	Fe	43	21 yrs.	5 yrs.	5/26/49	48%	91%	5/31/49	6/1/49		Dysphagia Some degree asthma	
7.	M	48	7 yrs.	3 yrs.	4/8/49	30%	72%	4/20/49 6/9/49	6/17/49	8/2/49	no asthma	
8.	Fe	25	7 yrs.	4 yrs.	2/9/49	59%	93%		4/19/49		Slight wheeze	Will do left denerv. late
9.	Fe	40	5 yrs.	2 yrs.	8/13/48	30%	70%	2/25/49	3/24/49	2/10/50	no asthma	
10.	M	43	43 yrs.	5 yrs.	6/15/49	66%	80%		7/12/49		no asthma	
11.	M	40	14 yrs.	2 mo.	4/6/49	32%	80%	5/29/49	6/30/49	9/29/49	no asthma	
12.	M	48	10 yrs.	1 yr.	7/1/49	50%	70%	7/5/49 9/29/49	10/11/49		no asthma	

TABLE I

CASE REPORTS

Table 1, lists data pertinent to each of twelve cases. Duration of residence in Arizona is given to illustrate the failure of benefit from climate. Vital capacity, expressed in percentage of normal, is recorded before and after use of an aerosol antihistaminic to indicate the degree of respiratory impairment due to bronchospasm. The dates of deep ether anesthesia and bronchoscopy reveal the periods of relative relief obtained.

COMMENT

Observation of the postoperative experiences of these cases indicates that the degree of relief depends to a great extent on the amount of pulmonary emphysema and impairment of "toilet" of the bronchial tree existing previous to operation. Further study of these factors may help in the more intelligent selection of cases. At present case studies include the use of the Collins respirometer and blood oxygen determinations with the oxyhemograph. This experience also shows the need for careful evaluation of the psychogenic factor in each case.

^oLeft denervation was done on February 20th. So far this patient is free of asthma.

SUMMARY

Experience with so-called pulmonary denervation in twelve cases of intractable bronchial asthma has been presented. The postoperative period is too brief to permit any conclusions. Four of the cases have had bilateral denervation. One case is to have a left denervation in the near future.^{o*} Seven patients are free of asthma so far. One patient died from an overdose of Demerol taken in a period of despondency of mild asthma. One patient has persistent mild wheezing, relieved by two minims of adrenalin. One patient had postoperative dysphagia and continues to have asthma.

This series of cases would seem to indicate that further study of the surgical relief of intractable bronchial asthma is warranted.

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FULL TERM ABDOMINAL PREGNANCY WITH INTESTINAL OBSTRUCTION

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Abdominal pregnancies have been reported with increasing frequency since Cornell and Lash³, in 1933, published a statistical review of 236 cases. Gardner and Middlebrook⁵ added 22 and Beacham and Beacham¹ added 20 more.

The following case is presented because of the complications of intestinal obstruction and the delivery of a normal viable infant. Longley⁶ reports that the fetal mortality is 67.3 in those that progress to term or in his review of 236 cases only 41 normal live babies were obtained.

Beacham and Beacham¹, in a report of twenty abdominal pregnancies from Charity Hospital at New Orleans, found that only 3 or 15 per cent delivered living infants.

Sutter and Wichser⁸, reviewed forty-one additional cases from the literature and found a specific statement as to the development of the baby in thirty-one. "Twelve or 38.7 per cent, of these babies were found to be deformed. Ten, or 24.3 per cent of the babies died before the eighth day and his conclusions are that one-fourth of all extra-uterine pregnancies diagnosed after the fifth month of gestation will result in viable babies. About one-third of all these living babies delivered from extra-uterine pregnancies will have major or minor deformities, including those which are incompatible with life. Approximately half of all living babies delivered from extra-uterine pregnancies will survive eight or more days".

Bland² reported a maternal mortality rate of 34.7 per cent for 240 cases of late extra-uterine pregnancy collected from the literature from 1813 to 1907.

Cornell and Lash³ reported a maternal mortality of 14.3 per cent in 236 cases and Ware⁹ reported a maternal mortality of 30.76 per cent in thirteen cases operated upon during the past fifteen years. The chief cause of death was hemorrhage and shock.

The diagnosis is difficult and was not made in this case prior to laparotomy. In the review reported by Gardner and Middlebrook⁵ of 258 cases, the diagnosis was made in 83 prior to operation; in 27 cases the diagnosis was normal pregnancy; in 16 cases, pregnancy and fibroid tumor;

in 15 cases, pregnancy and ovarian cyst. In the diagnosis of abdominal pregnancy the history in early pregnancy of tubal rupture is important. Roentgenograms may show a distorted fetus. Vaginal examination may show the cervix to be high and in an abnormal position to the presenting part. Lipiodol visualization of the uterus may be used to confirm the diagnosis.

The treatment of the placenta must be determined by the individual case. In the one reported the placenta was removed and this should be done if possible without endangering the life of the mother. In the cases reviewed by Gardner and Middlebrook⁵ the placenta was entirely removed in 162 cases, with 17 maternal deaths; partially removed in 11 cases with 2 maternal deaths; and left in situ in 48 cases with 10 maternal deaths. Adequate blood transfusions, absorbable hemostatic cellulose gauze, and improved anesthesia are a distinct aid in facilitating its removal. Several cases have been reported where it was necessary to remove the encapsulated placenta several months after the initial operation⁴⁻⁷. Marsupialization is generally condemned.

REPORT OF CASE

Hrs. L. H., aged forty-four was first seen for prenatal care in January, 1948. Examination at that time revealed an enlarged uterus, approximately the size of a two months gestation. No adnexal masses or tenderness were noted. The patient stated that her past history was essentially uneventful, with the exception of having had two pregnancies, the last nineteen years ago. These pregnancies were without complications. Her last menstrual period was on November 16, 1947. On December 31, 1947 the patient complained of acute lower abdominal pain with associated nausea and vomiting. She was seen by a physician and was treated for a threatened abortion. The pain subsided after a few days. On February 19, 1948 the patient again had severe lower abdominal pain, with associated nausea and abdominal distention. She was hospitalized and observed for a period of three days. Examination by the admitting physician this time revealed the uterus to be enlarged and softened. No bleeding was present. The abdomen was markedly distended and no adnexal masses were felt. The blood count

showed evidence of moderate secondary anemia (3,600,000) and the usual leukocytosis of pregnancy (12,550). Her temperature at this time was elevated for two days to 100 degrees. After her discharge from the hospital her prenatal course was uneventful until the last trimester. Her only complaint was that of constipation.

On September 1, 1948, or nine days after her expected date of confinement the patient was hospitalized for hypertension and albuminuria. Her blood pressure was 180/100 and urine examination showed a trace of albumin. The patient's only complaint was slight headache. Abdominal examination revealed a full term pregnancy. The vertex was presenting above the pelvic brim, the fetal heart rate was 140. On rectal examination the fetal head could be palpated high in the pelvis. No engagement was present. No abdominal contractions or tenderness were noted. Because of the position of the head and its failure to engage in the inlet of the pelvis, an roentgenogram of the abdomen was made. The report was as follows, "A mature fetus, near term, with the head obviously high and not engaged but what is a grossly normal appearing pelvis ample in all respects. It is apparent, however, that there must be some non-opaque obstruction of some type which does not allow the fetus to properly be engaged. In its present position the spine and occiput are to the right and the head lies to the right of the midline".

Approximately 36 hours after admission the patient suddenly developed severe continuous pain in the right side of her abdomen, more severe in the right flank and right upper quadrant. Abdominal examination showed no uterine contractions or rigidity; fetal heart sounds were normal; blood pressure was 140/90. The patient was observed for evidence of an acute abdomen. Twelve hours later the patient showed moderate abdominal distention, blood pressure was 140/90 and the pain was moderately severe in the same location. The picture was that of a low bowel obstruction, the distention became more pronounced, the patient failed to expell flatus and increased intestinal peristalsis was noted. A Barium enema was taken and the roentgenogram reported as follows; "Barium very slowly fills the rectum which distends before it can be forced through the sigmoid. It is seen that the sigmoid is moved toward the midline by the previously described non-opaque mass in the lower left quadrant. The sigmoid is primarily involved but is attenuated as it is stretched up over the mass. Barium is forced beyond this point of attenuation and narrowing in small amounts and it was deemed wise to go no further. It is obvious that the previously described non-opaque obstruction in the left flank is in the nature of a mass which is causing a partial obstruction due to its impingement upon the adjacent sigmoid which is moved toward



Figure 1

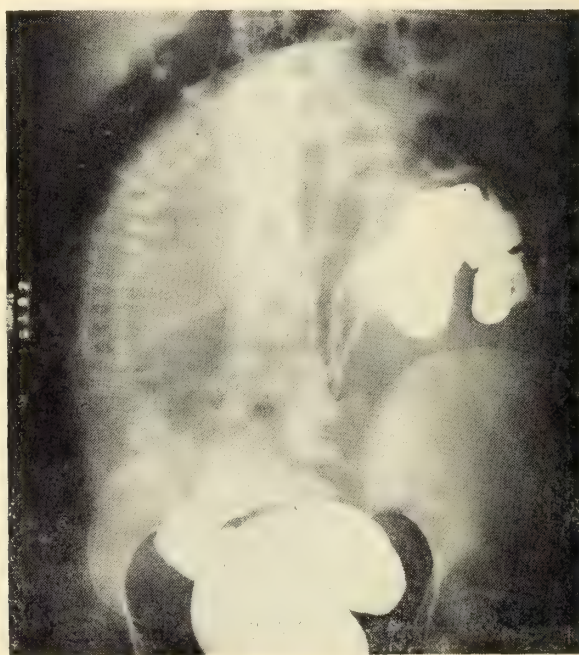


Figure 2

the midline. This same obstruction may well account for the fact that the fetus is held high and displaced to the right. The nature of the mass cannot be identified from these films".

In view of the physical findings and x-ray examination preparation for abdominal laparotomy was made. The preoperative diagnosis was intestinal obstruction due to lower abdominal tumor which also prevented engagement of the head. It was thought that this was a cyst or uterine fibroid. The abdomen was opened with a lower midline incision; a moderate amount of bloody serious fluid was first noted. A large apparently hemorrhagic cyst was present which was incised and the fetus delivered. The infant cried spontaneously. The origin of the sac in the left iliac fossa was adherent to the surrounding omentum and intestine. With the delivery of the fetus a large amount of bleeding started from the diffuse placenta, which was extremely friable, arising from the iliac fossa, extending into the region of the left broad ligament, and encrouched upon the sigmoid. Because of the profuse bleeding the fragments were removed as rapidly as possible and bleeding controlled by numerous pieces of cellulose gauze sutured over the bleeding surfaces. All bleeding was controlled in this manner. Examination of the uterous and adnexa showed no evidence of previous rupture or injury. The uterus was enlarged to the size of a three month's gestation. Blood was given continuously during the procedure and the patient showed no signs of undue shock. The abdomen was closed in layers. A rubber tissue drain was placed

in the left iliac fossa and brought out through a stab wound. Post-operatively the patient was given anti-coagulants and penicillin. Her course was uneventful and the patient was discharged from the hospital on the tenth post-operative day. Examination after six weeks and again three month post-partum showed normal involution of the uterus with no residual adnexal masses or tenderness. Her menstrual periods resumed there regular cycle.

SUMMARY AND CONCLUSIONS:

A full term abdominal pregnancy with intestinal obstruction and the delivery of a normal viable infant is reported.

The placenta should be removed when possible to obviate a second operation to remove the ensapsulated placenta which is not always absorbed. The use of absorbable hemostatic cellulose gauze was found to be a valuable aid in controlling the hemorrhage and facilitating the complete removal of the placenta.

The intestinal obstruction produced by the abdominal pregnancy precipitated the operation that may have saved the patient's life.

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BASIC SCIENCE SEMINAR

PROTEIN FRACTIONS IN HUMAN BLOOD PLASMA

By

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Introduction

The word "protein" is of Greek derivation meaning "I take the first rank". Mulder gave the name of "protein" to what he considered the

commencement, and starting point of all other tissues, because these are all produced from the blood.

Plasma is, of course, the end product of blood after the cellular elements have been centrifuged out. Plasma thus contains, three protein fractions, namely serum albumin, serum globu-

lin, and fibrinogen. Blood serum is blood plasma minus the fibrinogen fraction which has been removed in the process of clotting.

The studying of plasma protein chemistry is, in reality, only in its youth. The first amino acid, cystine, was first described by Wollaston in 1810. Liebig in 1842 wrote a paper to the effect that blood contained 2 ingredients, namely fibrin which is identical in all its properties to muscle fiber, and albumin, which is contained in the serum, and which has all the properties of egg white (5). Later globulins were discovered by Denis, a French physician, as methods of fractionation were devised. The greatest advances in blood protein chemistry have probably been made by Dr. E. J. Cohn, and his group, at Harvard, Boston, in the last ten years, proving that the chemistry of blood proteins is still in its infancy.

Classification and Origin

There are two different recognized classifications of proteins—the American, and the English. The differences between the classifications are only very slight, so that the American classification with its three large protein groups will be considered here (16).

1. Simple Proteins—

- albumins—serum albumin
- globulins—serum globulin, fibrinogen
- prolamines
- albuminoids
- histones
- protamines

2. Conjugated Proteins—

- nucleoproteins
- glycoproteins or glucoproteins
- phosphoproteins
- chromoproteins—hemoglobin
- lecithoproteins
- lipoproteins

3. Derived Proteins—

1. Prim.—

- coagulated proteins
- proteans
- metaproteans

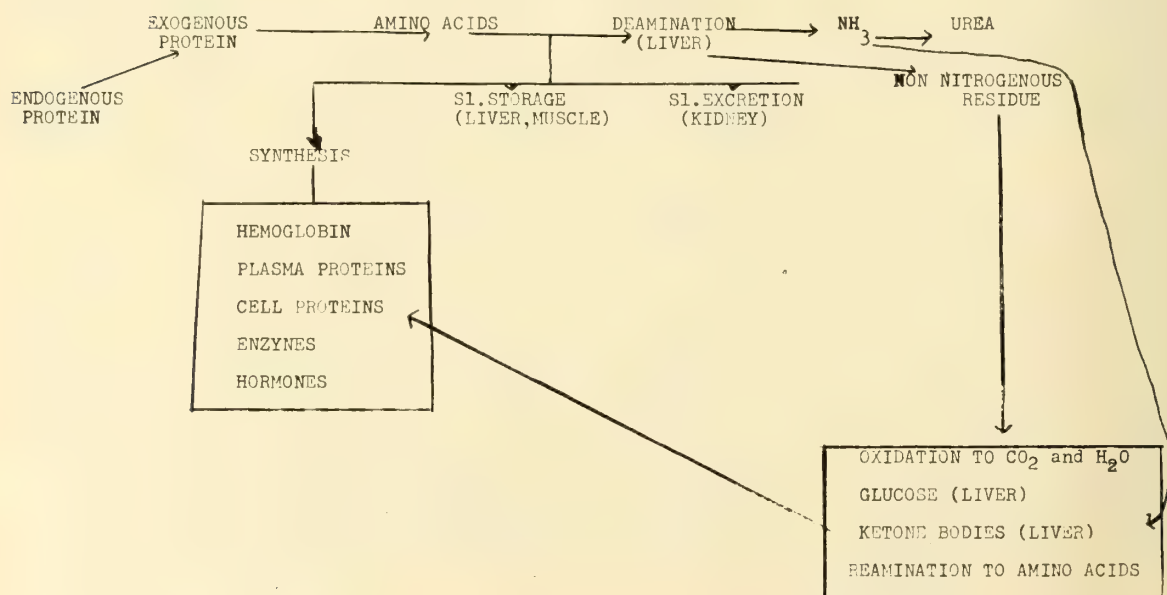
2. Sec.—

- proteoses
- peptones
- peptides
- dihetopiperazines

Thus the plasma proteins are classified as simple proteins, namely albumins, and globulins. The fibrinogen is also classified as a globulin.

The plasma proteins are synthesized in some way from amino acids (see diagram re protein metabolism). It is felt that fibrinogen (2) is produced in the liver, as proven by the reduction of this substance in liver damage or hepatectomy. There are six possible origins of the serum albumin, and globulin. They may be produced from disintegrating blood cells, the general tissue cells, the liver, the reticulo-endothelial cells of the spleen, or of the bone marrow, and perhaps from the intestinal mucosa. For years the liver was favored as the organ of production of these substances, but it is now

OUTLINE OF PROTEIN METABOLISM (4)



felt (13) that the globulins may at least be partially formed from the plasma cells, and the cells of the reticulo-endothelial system. There are no protein depots in the body as for carbohydrate and fat. Thus reserves are found (1) in the labile cytoplasmic protein, making up the plasma, hepatic, and muscular tissues of the body.

It has also been shown that the lymphocytes (12,40) in the lymphoid tissue are the storehouse for a portion of the globulin fraction of plasma—chiefly the gamma globulin, and possibly also the beta globulin. This globulin is mobilized and liberated into the blood stream by adrenal cortical hormone, and by A.C.T.H. through stimulation of the adrenal cortex. Administration of these hormones is followed by degeneration and atrophy of the lymphatic tissue, lymphopenia, apparently due to the dissolution of stored lymphocytes, and an increase in the plasma globulin. There is a simultaneous increase in the rate of release of antibody from lymphoid tissue (gamma globulin) indicating that serological defense reactions are partly under control of these pituitary and adrenal hormones.

Fractions and their Properties

Human blood is composed of 91% water, and 9% solids. The plasma proteins make up on the average 7:1 gms. per 100 cc of the total 9 gms/ per 100 cc solids.

Prot. in Human Plasma (2) Rge Av. (Gms./100 cc)			
Total Plasma Protein	6.— 8		7.1
Fibrinogen	.20 — .40		.27
Serum Globulin	1.3 — 3.2		2.7
Serum Albumin	3.6 — 5.6		4.1
Ratio of 3 fractions	1:10:15		
A/G Ratio	3.2 or 1:5		

These figures are fairly constant for healthy humans. There is however, a discrepancy in the total plasma protein from birth to the age of four months. At birth, the total plasma protein level averages 5.9 gms. per 100 cc (36); at one month of age it is about 5.5 gms., and it only reaches the average adult level of 7.1 gms. at four months of age.

The plasma proteins were first fractionated into three substances—serum albumin, serum globulin, and fibrinogen. By more careful methods of fractionation, using a salting out procedure with either sodium sulfate, or alcohol, the serum globulin was subdivided into euglobulin, and pseudoglobulin I and II (4).

Later Tiselius (18) in Svedberg's laboratory, by using an ultra-centrifuge, and electrophoretic

methods was able to separate the serum globulin into alpha, beta, and gamma fractions.

Recently Cohn of Boston (5) by methods of electrophoresis and sedimentation time, has been able to fractionate the plasma proteins into six large fractions. He has also proven that there are several different alpha and beta globulin factors in human plasma. His classification is as follows:

Fraction I—contains most of the fibrinogen (60-90%) and the antihemophilic globulin.

Fraction II—contains the gamma globulin antibodies of proven value in the prophylaxis of measles, and probably also of infectious hepatitis.

Fraction III—1—contains other antibodies including those to typhoid O, the isoagglutinins, including the anti-Rh antibodies.

Fraction III—2—contains prothrombin, and one of the components of complement.

Fraction III—3—contains plasminogen, the precursor of plasmin, the fibrinolytic enzyme.

Fraction III—0—is rich in Lipoprotein (beta 1 globulin)

Fraction IV—1—also contains lipoprotein (alpha 1 globulin)

These lipoproteins in Fraction III—0 and Fraction IV—I are bearers of cholesterol, carotene, and such steroids as estriol and vitamin A.

Fraction IV—4—contains a variety of enzymes, and hormones including hypertensinogen, thyrotropin, and a serum esterase.

Fraction V—contains human serum albumin.

Fraction VI—contains large amounts of salts especially citrates, and a small amount of protein.

Each of the three main proteins in plasma protein is a simple protein. Fibrinogen has a molecular weight of 200,000. It has been isolated in crystalline form, and X-ray diffraction studies indicate that its molecule is structurally similar to that of collagen. Its concentration is low, and thus it contributes little toward the total osmotic pressure of the blood.

Albumin has a molecular weight of 70,000—75,000. It is soluble in water, and dilute salt solution; it is also coaguable by heat. Since it makes up the highest concentration in plasma, the osmotic pressure, therefore depends largely on this fraction.

Globulin has a molecular weight of 150,000—190,000. It is insoluble in pure water, but soluble in dilute neutral solutions of salts of

strong bases and acids. Normally its concentration is less than that of albumin.

Functions of the Plasma Proteins (2)

1. Fibrinogen is essential for the clotting of blood.

Prothrombin plus Thromboplastin plus Ca yields Thrombin

Thrombin plus Fibrinogen yields Fibrin.

2. All three serve to maintain the osmotic pressure of the blood.

It is to be noted that the pressure which each fraction exerts is inversely related to the size of the molecule, and directly related to its concentration in the plasma.

Thus the albumin which has the highest concentration, and the least molecular weight, exerts the greatest osmotic activity.

3. The plasma proteins give a certain viscosity to the blood which is a factor in the maintenance of a normal blood pressure.
4. They aid in the acid base balance of the blood.
5. The globulin, and fibrinogen fractions tend to influence the stability of the blood by causing the corpuscles to adhere to one another, and form rouleaux or clumps.
6. They contain substances from which leucocytes prepare trephones which are essential for the nourishment of tissue cells grown in cultures.
7. They contain immune substances which are associated with the globulin fraction, and which are increased during the process of immunization.
8. They serve as a reserve of protein upon which the body draws during fasting, or when the protein intake is inadequate (28).

Clinical Diagnostic Value

The average value of the plasma proteins is between 6.0 to 8.0 gms. per 100 c.c's. The concentration of the serum albumin is much more than that of the serum globulin by a ratio of 3.2. The albumin is affected much more readily than the globulin by the protein intake, while the globulin is regenerated more quickly than the albumin following hemorrhage (4). As a generalization it can be stated that the albumin fraction is rarely increased above normal, and the globulin fraction rarely decreased below normal.

Moore and Van Slyke (27) state that patients will develop non cardiac edema when the total plasma protein falls below 5.5+3% or when the albumin fraction falls below 2.5+2%.

1. Low Total Plasma Proteins (Hypoproteinemia)

This may occur because of one or more of three causative factors:

- A. Inadequate supply of protein.
- B. Impaired synthesis of protein.
- C. Excessive protein catabolism.

Inadequate supply of protein may cause such clinical conditions as war edema, famine edema, and nutritional edema. Here inanition is the causative factor. It is also a factor in the low total plasma protein seen in far advanced tuberculosis, and malignancy. It is seen too in gastrointestinal disorders accompanied by impaired protein digestion or absorption, prolonged vomiting or diarrhea, such as peptic ulcer, G.I. malignancy, pancreatic disease, intestinal fistula, short circuiting operations on the intestines, chronic ulcerative colitis, tuberculous and chronic enteritis, congestive heart failure with edema of the G. I. mucous membrane, and pellagra.

A low total plasma proteins due to impaired synthesis occurs in the following condition:

1. Chronic hepatic disease
2. Chronic glomerulonephritis
3. Various infections
4. Severe anemias (uncontrolled pernicious anemia).
5. Cachectic states
6. Pregnancy and lactation (25)

It is especially true in eclampsia and pre eclampsia.

A low total due to excessive protein catabolism may be found in uncontrolled diabetes mellitus, and severe thyrotoxicosis.

II. Hyperproteinemia

An increased total plasma protein occurs usually in dehydration. However, in many cases where dehydration is a factor, complication factors such as inanition, diarrhea, and vomiting, exert an influence which tends to decrease the plasma protein concentration. However, in the following cases, a total plasma protein of from 10.-12. gms. per 100 cc, have been reported.

1. Cholera—infant diarrhea
2. Shock
3. Burns
4. Diabetic acidosis
5. Addison's disease
6. Intestinal obstruction
7. Heat exhaustion.

III. Hypoalbuminemia

A decrease in the albumin fraction of the plasma proteins is usually associated with a compensatory increase in serum globulin, and

occasionally fibrinogen. A decrease in the serum albumin is found in the following conditions:

1. Nephritis
2. Nephrosis
3. Amyloid diseases of the kidney.
4. Congestive heart failure
5. Multiple myeloma
6. Chronic hepatic disease
7. Extensive burns.
8. Pick's disease (polyserositis)
9. Intestinal obstruction
10. Generalized peritonitis.

In chronic nephritis as much as 60 gms. of albumin may be eliminated per day. A daily loss of 4-5 gms. may result in a gradual decrease in the level of the plasma protein. Van Slyke found that cases of this condition which maintained plasma albumin values above 2.2 gm. per 100 cc or total protein values above 5.5 gm. per 100 cc have a better prognosis than those which do not. Thus the plasma protein concentration is of prognostic significance during the acute stage of glomerulonephritis. Also a low plasma protein concentration, usually below 2.5 gm. per 100 cc is the rule in diagnosing the chronic active stage of glomerulonephritis. As the chronic active stage progresses into the terminal stage, there is a marked tendency for the plasma proteins to increase, normal values being obtained in about half the cases during the terminal stage of the disease. This may be due in part to decreased albuminuria, and in part to hemoconcentration.

In chronic renal disease, the decrease in plasma protein is due to three factors—albuminuria, a nutritional defect which interferes with the ability of the organism to regenerate serum albumin, and malnutrition (a lack of adequate protein intake).

In nephrosis the globulin and fibrinogen are commonly markedly increased—the former rising to 5 gm per 100 cc and the latter going as high as 1 gm. per 100 cc.

The hypo-albuminemia seen in extensive burns, intestinal obstruction, and generalized peritonitis is due to the loss of plasma from the circulation (14).

IV. *Hyper-Globulinemia*

In general the alpha globulins increase in febrile conditions; the alpha and beta globulins increase, while the gamma globulins decrease in chronic nephrosis (6). The beta and gamma globulins increase in multiple myeloma, while

the alpha and gamma globulins increase in tuberculosis. There is a close correlation between the sedimentation rate, and the alpha globulin concentration. Both increase in the presence of considerable tissue destruction or inflammation (31). Hyperglobulinemia with or without hyperproteinemia occurs in the following conditions:

1. Certain acute and chronic suppurative conditions.
2. Lymphopathia venereum.
3. Multiple myeloma
4. Boeck's sarcoid
5. Certain miscellaneous conditions.

There is evidence which suggests that the maintenance of a high plasma globulin concentration is responsible for the development of amyloid disease in conditions associated with chronic suppurative processes.

In multiple myeloma, the hyperglobulinemia is present in 50-60% of cases (3). The beta and gamma globulins increase, and there is also some suggestion of the presence of a Bence-Jones protein in the serum.

The miscellaneous conditions include malaria, leukemia, syphilis, rheumatoid arthritis, filariasis, tuberculosis, lupus erythematosus periarteritis nodosa, leprosy, and kala-azar.

V. *Hypo-albuminemia and Hypo-globulinemia*

This combination of a low serum albumin and a low serum globulin is the exception to the rule and is only seen in children with either coeliac disease, or far advanced malnutrition.

VI. *Fibrinogen Fraction*

The normal value of fibrinogen is from 200-400 mgms. per 100 cc. It is increased in the following conditions:

1. Slight hepatic injury (hepatitis)
2. Most acute infections (except typhoid fever)
3. Pregnancy and menstruation
4. Following X-ray radiation.
5. Focal infections—sinusitis, tonsillitis
6. Nephrosis
7. Multiple myeloma
8. Lymphopathia venereum.

In nephrosis the fibrinogen may be up to 1000 mgms. per 100 cc in order to compensate for the decrease in serum albumin. The increase here, as in the case of acute infections, is made possible by the existence of a generalized increased cellular permeability, allowing the more ready entrance of the comparatively large fibrinogen molecule into the circulation.

Fibrinogen is decreased in the following conditions:

1. Hepatic insufficiency.
2. Typhoid fever.
3. Following severe hemorrhage—temporary.
4. Cachetic conditions.
5. Constitutional fibrinogenopenia.

In this latter condition there may be a delayed coagulation of blood, or profuse bleeding after slight trauma due to an inadequate amount of fibrinogen (30). The fibrinogen is also occasionally decreased in pernicious anemia, pellagra, scurvy, myelogenous leukemia, and other diseases of the bone marrow (41).

Use in Diagnostic Reactions

Many liver function tests depend on reactions (usually chemical) involving either the serum globulin or the A/G ratio.

The Takata-Ara Reaction (23) is positive due to an increase or qualitative abnormality in the globulin fraction. It is positive in portal cirrhosis, and other forms of severe hepato cellular damage.

The Formol-Gel Reaction (2) is positive in conditions accompanied by a significant hyperglobulinemia. Thus a positive reaction is obtained in the same conditions as the Tahata-Ara Reaction is positive.

A paretic type of colloidal Gold Curve (21) is produced by some qualitative or quantitative change in the euglobulin or gamma globulin fraction. This curve is seen in portal cirrhosis, portal necrosis, hepatitis, and portal malignancy.

The Cephalin-Cholesterol Flocculation Test (14) depends on one of three factors for its positivity:

1. An increase in the gamma globulin in such quantity that the normal components of the serum albumin fraction are unable to inhibit the reaction.
2. A decrease in the serum albumin concentration below that capable of inhibiting the reaction.
3. A decrease in the flocculation-inhibiting properties of the serum albumin fraction due to its chemical modification.

Thus the Cephalin-Cholesterol Flocculation Test is positive in a large proportion of cases of active hepato-cellular disease.

The Thymol Turbidity Test (22) gives results parallel to those obtained with the Cephalin-Cholesterol Flocculation Test. The only difference is that it gives a positive response in

lipemia sera. Thus it is positive not only in many cases of active hepatocellular disease, but also in diabetes mellitus, and nephrosis.

Weiss (38) has devised an excellent method in determining the amount of liver damage in cases of liver disease. This determination is based on different shifts of the A/G ratio. The test itself is based on three separate determinations of the blood protein-albumin, globulin, and fibrinogen, and three complete blood counts.

The procedure in the test is as follows:

1. Bed rest with no food.
2. 6 cc. oxalated blood is drawn for determination of plasma proteins, and C.B.C.
3. A mixture composed approximately of $\frac{1}{2}$ liver, $\frac{1}{4}$ stomach mucosa, $\frac{1}{8}$ pancreas, and $\frac{1}{8}$ spleen. After a skin test is performed, 1 cc of the above mixture is injected deeply into the gluteal muscle.
4. The injection of 1 cc of mixture brings about a rapid shift of the blood proteins and corpuscles in one to two hours. The lower the A/G ratio, with globulin being the denominator, the more affected is the liver function. A shift in the blood count is advantageously used for prognosis, a decrease in lymphocytes being a favorable sign, and an increase in the number of lymphocytes indicating a poor prognosis.
5. 6 cc of blood withdrawn one hour after injection.
6. 6 cc of blood withdrawn two hours after injection.

The results depend on one of five different shifts of the A/G ratio, and may be interpreted as follows:

- (a) When the A/G ratio changes only within its physiological range, i.e. less than 0.1 of its value, liver function is normal.
- (b) When the A/G ratio increases after one hour, and again after two hours, liver function is slightly affected.
- (c) When the ratio increases after one hour, and decreases after two hours, liver function is moderately affected.
- (d) When the ratio decreases after one hour, and increases after two hours, liver function is markedly affected.
- (e) When the ratio decreases after one hour, and again after two hours, liver function is seriously affected.

Therapeutic Uses of the Serum Albumin

Normal human serum albumin was primarily

(20) developed as a blood substitute for use in traumatic shock. It is to be noted that concentrated albumin, unlike concentrated plasma or gelatin is only as viscous as whole blood with a hematocrit reading of 50% (7), and when injected, it lowers blood viscosity due to hemodilution. That is why it is more readily tolerated by patients with mild congestive failure than whole blood, or other more viscous colloidal solutions. It may be used in the following conditions:

1. In the treatment of shock.
2. In the treatment of hypoproteinemia with edema
 - (a) Chronic nephritis.
 - (b) Chronic nephrosis.
 - (c) Chronic cirrhosis.
3. In the treatment of acute nephritis.
4. In the treatment of toxemias of pregnancy.

In the treatment of shock, albumin appears as to be an effective blood substitute. Studies in circulatory dynamics in shock patients receiving albumin showed that improvement after albumin therapy was associated with an increase in cardiac output which was greater than that produced by the administration of whole blood (8).

The serum albumin is distributed in 25% solution, and in the treatment of burns, hemorrhage, or trauma in patients with decreased blood volume, it produces both clinical improvement, and a considerably greater increase in the plasma volume than can be accounted for by the volume of the solution injected. Saline enhances the effect of the albumin. A 5% albumin solution in 0.85% saline solution is approximately isosmotic, and isotonic with citrated human plasma. Thus each 100 cc of 25% albumin solution should be supplemented with 400-500 cc N. saline solution when possible, in the treatment of shock. This may be given by vein, or by mouth.

Hypoproteinemia is associated with chronic Bright's disease (35) has been treated with some success with salt poor concentrated human serum albumin. The dosage used has been 50 gms per day over a period of twenty to thirty days. Since the serum albumin is salt free, it is given in 10% glucose solution. Following the first dose, there is an increased urine output associated with an increased excretion of protein, chloride, phosphorus, and non-protein nitrogen. There is a slight increase in the serum albumin level. This

treatment works best on massive edema cases, and produces no response in non-edema, or minimal edema cases. Its value is that it affords transient symptomatic treatment.

Serum albumin may be used in acute nephritis, and acute sulfadiazine intoxication producing acute renal failure, to maintain an adequate serum protein level without elevation of the N.P.N. provided sufficient calories are administered to spare protein catabolism. This is in line with the present feeling that the best treatment for anuria is to keep the chemical composition of the body fluids as normal as possible by parenteral and oral administration of carbohydrate, fluid electrolytes (29) under rigid laboratory control. Thus the patient is kept alive until spontaneous repair of the renal lesions leads to a return of the excretory function.

There is excreted a large amount of serum globulin, and serum in pre-eclamptic patients (11). It also appears that the serum protein level may be a better index of the severity of pre-eclampsia than the uric acid determination. In keeping with this statement is the fact that anuria is a sign of seriousness, and that unless diuresis can be effected, improvement usually fails to take place. Salt poor serum albumin in a dose of 25 gms every six hours is a potent therapeutic aid in the treatment of anuria by increasing the blood volume, and decreasing the viscosity—thus enhancing the filtrable activity of the glomeruli (34). This serum albumin should be used in conjunction with the standard treatment of pre-eclampsia. Dorr also feels that if a patient does not improve with that treatment within twelve to thirty-six hours, or if after improvement there is a return of symptoms or clinical findings, delivery should be consummated.

Therapeutic Use of the Globulin Fraction

Pooled gamma globulin (33) refers to the gamma globulin from large pools of adult blood plasma. By fractionating this pooled plasma by a method first developed by Dr. E. J. Cohn and his co-workers (7) at Harvard medical school, a gamma globulin fraction was obtained (15) which has a concentration in antibodies of about 25 times that of normal pooled plasma. Thus the uniformity of antibody levels in pooled plasma, and thus in gamma globulin depends chiefly upon the following factors:

1. The presence of endemic or recent epidemic disease in the geographical area from

which the blood is drawn.

2. The amount, and duration of antibodies resulting from specific infections.
3. The number of donors contributing to the pool.

A combination of Fraction I and thrombin has been used to promote adherence of skin grafts (9), and to form a coagulum (10) around calculi in the renal pelvis so as to effect their complete removal without fragmentation. In the form of fibrin foam with thrombin, the clotting proteins have been widely and successfully used to accomplish rapid hemostasis in neurosurgical, and certain other surgical procedures. The anti-A, and anti-B isoagglutinins and the Rh globulin derived from Fraction III-1 by concentration of this activity from pooled group-specific or anti Rh plasma (24) provide dependable reagents for grouping blood which should increase the safety of transfusions of either whole blood, or of resuspended red cells.

The gamma globulins have come into importance in recent years because of its value in attenuating and preventing certain diseases. Its value has been investigated in the following diseases:

1. Measles
2. Mumps
3. Scarlet fever
4. Infectious hepatitis
5. Poliomyelitis

It is felt in pediatric circles that children under five years of age should be either attenuated or protected against measles, and that children under two years of age should definitely be protected against the disease because of the severity of certain complications. In Great Britain and Canada, convalescent measles serum is used almost exclusively in the prevention or attenuation of measles, while in America gamma globulin is used. For attenuation 2.5 cc of convalescent measles serum, or 1.2-1.5 cc of gamma globulin is the usual dosage (19). For protection 5.0 cc of convalescent measles serum is required, or 3.5 cc of the gamma globulin is used. 91-92% of patients, using either therapeutic agent obtain attenuation.

In the protection line, 70% are protected using convalescent measles serum, while 82% are given protection by the gamma globulins. The dosage of gamma globulin recommended for protection is 0.1 cc per pound body weight given intramuscularly as soon as possible after the first

exposure to the infection. However, large doses of gamma globulin administered in the prodromal stage of the disease, at or previous to the appearance of Koplik spots, also apparently modify the disease (33).

The value of gamma globulin in mumps appears to depend upon facilities for the pooling and fractionation of large amounts of convalescent plasma (33). The injection of ordinary gamma globulin produces no significant effect. However, the injection of 20 cc of gamma globulin from convalescent pools produced a decrease of from 8-33% in the incidence of orchitis. Thus if the pooled gamma globulin is obtainable, it should be reserved for the treatment of adult males in the first twenty-four hours of the disease, with the aim of preventing or attenuating acute orchitis, thus decreasing the high incidence of sterility in the male following mumps and orchitis.

Gamma globulin has also been used in the treatment of scarlet fever (32). In mild cases of scarlet fever the use of gamma globulin, in doses of 1 cc per pound body weight up to a total of 60 cc, appears to attenuate the disease more than the use of antitoxin alone. However, in severe toxic cases of scarlet fever, scarlet fever antitoxin should be used.

Stokes (33) feels that gamma globulin is beneficial in the prevention of infectious hepatitis in doses of .06 cc per pound body weight, but that it was of no value in the treatment of the active disease. Injections of gamma globulin in the prodromal pre-icteric stage or in the acute stage, fails to attenuate the infection (37). It was found that gamma globulins confer temporary benefits on the long chronic type of infection in doses of 20 cc per day on alternate days.

The effects of gamma globulins in poliomyelitis has also been tested and Stokes (33) has come to the conclusion that gamma globulin injected during the incubation period, or in the preparalytic stage has no effect on the course or the outcome of the disease.

Therapeutic Use of Fibrinogen

In the studies of Cohn's fractions, it was shown that Fractions I, II, and III had marked antihemophilic activity. Since Fraction I contains from 60-90% fibrinogen, it is used as the best source of antihemophilic potency. Fraction I is available in vials of 200 mgms; it is in powder form, and is injected intravenously after being dissolved in 50 cc of sterile distilled water.

In fifteen to thirty minutes, 200 mgm will lower the venous coagulation time in hemophilia toward normal, and its effect will last about four hours (39). This treatment is better than blood transfusion in hemophiliacs, as it lowers the coagulation time much more. Thus it is of value in hemophiliacs in extracting teeth, in surgery, and in the stopping of hemorrhage from a wound.

Conclusion

In this review of plasma protein chemistry, an attempt has been made to summarize the advances made in this subject since its beginning in 1842 up to the present time. It is also designed to show that there is still much investigation to be performed before the complete story is unfolded.

Also, I would like to thank Dr. A. C. Van Ravenswaay and Dr. M. G. Vavich for their kind assistance in helping me prepare this paper.

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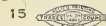
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2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

Editorials

ELECTROLYTE BALANCE

Our knowledge of tissue fluid chemistry has taken a great stride forward with the employment of isotopes to trace the fate of less well known chemicals during their journey through the body. Many inexplicable untoward results of supposedly good therapy now become understandable. But since there is a considerable time lag between the discovery of a significant biochemical fact and its employment by the clinical

cian needless deaths still occur—preventable deaths.

A great advance in proper therapy was the then new avenue of fluid administration, namely hypodermoclysis and venoclysis. Subsequently there was added to the isotonic salt solution glucose, and still later other substances such as proteins, vitamins, blood, and antibiotics. The disappointing results obtained with these solutions in certain cases led to the discovery that saline solution is of itself toxic if used in excess, and that too much of it in the body led to dilution of the already depleted other rarer electrolytes, and the effort of the body to wash this excess out through the kidneys further depleted other ions that the ill body could scarce afford to lose. It is to be recognized that saline simply replaces sodium and chlorides and glucose is simply a food for quick energy but is in no form an electrolyte. Yet too many of us still restrict the parenteral fluids to 5% Glucose in saline solution.

The dehydrated patient, and this refers equally to surgical as well as medical patients needs singly or in various combinations, red cells, plasma proteins, water, Sodium, Chlorides, Bicarbonates, Potassium, Phosphorus, Amino Acids, Dextrose, and Vitamins. The dehydrated patient is especially short on intercellular potassium which was lost with acidosis and loss of fluids. The rapid replacement of total tissue fluids with Saline solution simply dilutes the reduced potassium present. If, however, potassium is infused into the blood stream too rapidly as by intravenous use of it instead of sodium, untoward results again ensue. The intercellular potassium diffuses into the cells very slowly, and an excess of intercellular potassium, even tho the cells are depleted, will lead to cardiac damage. On the other hand, a loss of potassium without replacement will lead rapidly to death, as is seen in certain cases of diabetic acidosis and coma who die because of the lack of potassium. This is but a single example of the vital need for a clear understanding of the significance of proper electrolyte balance.

Lately there has been too great a tendency to give intravenous fluids. We all see on hospital wards patients perfectly able to retain oral fluids sitting upright in bed getting an intravenous feeding, with the fluid running in at a greatly excessive speed. This massive flooding of the circulation is both dangerous and waste-

ful, expensive and messy. A lucid patient who has no difficulty swallowing and is not vomiting may very well take his fluids orally with a lot less expense and trouble.

The key to correct judgment and proper use of our newer knowledge depends entirely on the laboratory reports of the status from day to day of the electrolyte values. It must therefore be an expensive but rewarding procedure—and utterly essential that daily or even hourly check be made on the progress of each case. The intelligent use of the laboratory reports will save lives. Clinical judgment is here emphatically not enough.

P. L. S.

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PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL HOSPITAL CASE NO. 29011

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A fifty-six-year-old author came to the hospital because of crampy abdominal pain, nausea and vomiting.

Beginning six months prior to admission he was often awakened because of crampy abdominal pain that was usually followed by nausea and at times by vomiting. During the day he usually felt better, but was bothered by "bloating" eructations and belching. An x-ray study done one month later demonstrated "colitis." One month before entry he developed constipation and often passed large amounts of gas by rectum. These symptoms were particularly noticeable since, following the resection of a fistula-in-ano fifteen years previously, he never had been completely continent of feces and movements tended to be loose. Five days before admission he became very constipated and suffered with extreme abdominal cramps, and subsequently his abdomen became distended. His physician treated him with repeated enemas, and some relief followed explosion of gas. Three days later he began to vomit a thin fluid, which did not contain blood or coffee grounds and did not have a fecal odor. He had never noted

tarry, bloody or alcoholic stools and had never been jaundiced. During the three months prior to admission he lost twenty pounds. For many weeks he was accustomed to drink as much as a pint of rye whiskey each day "to relieve nervousness and insomnia," but this was discontinued during the week prior to admission.

The family and past histories were noncontributory.

Physical examination revealed a very ill, dehydrated man who grunted with each breath. The mucous membranes were pale, dry and cracked. Examination of the heart and lungs was normal. Both diaphragms were elevated to the fourth rib anteriorly, and chest movements were limited. The abdomen was enormously distended and tympanitic throughout. The peristaltic sounds were weak and almost absent. No masses were felt on rectal examination, and sphincter control was absent.

The blood pressure was 122 systolic, 80 diastolic. The temperature was 99.1°F., the pulse 94, and the respirations 21.

Examination of the blood revealed a hemoglobin of 10.5 gm., red-count of 3,060,000 and a white-cell count of 16,700. The urine was cloudy, amber and acid in reaction, had a specific gravity of 1.010 and negative tests for diacetic acid, acetone and bile; one plus test for albumin; a rare red cell, 10 white cells and 4 epithelial cells per high power field; the sugar test was negative. The serum nonprotein nitrogen was 122 mg. per 100 c.c. the chloride 94.6 milliequiv. per liter, and the protein 4.9 gm. per 100 c.c. The stool was guaiac negative.

A flat plate of the abdomen demonstrated considerable gas in the dilated stomach and in numerous loops of small bowel, and probably a small amount of gas in the nondilated ascending and transverse colon. There was a large area of calcification overlying the fifth lumbar vertebra.

Many unsuccessful attempts were made to pass a Miller-Abbott tube into the small bowel. Accordingly, after glucose and saline infusions and plasma transfusions, under novocain infiltration, the abdomen was entered through a small oblique incision just to the left of the rectus muscle in the lower quadrant. The abdomen was explored with two fingers, and a hard mass was found approximately in the midline near the promontory of the sacrum. It was stony hard and was thought to represent the calcified mass

of lymph nodes seen in the x-ray. A small tag of omentum presented into the wound and on this were numerous small gray areas suggesting fat necrosis. There was considerable straw-colored free fluid in the peritoneal cavity. A loop of small bowel was drawn into the wound and a Witzel-type enterostomy was established. The biopsy of omentum showed fat necrosis.

Three days later, the patient seemed slightly improved. The distention was definitely reduced, and the respirations were slower and easier. Peristaltic sounds were more normal on the third hospital day. He was started on a course of intravenous sodium sulfadiazine, totaling 25 gm. in five days. On the sixth hospital day the liver edge was felt three fingerbreaths below the costal margin and seemed rough and uneven. At this time there was definite dullness and consolidation above the high diaphragm on the right side, with increased transmission of breath and voice sounds and occasional rales. The temperature was 99.8°F., the pulse 98, and the respirations 25. The decompression tube was draining a yellowish-brown fluid, although it had not passed the pylorus. A portable flat plate of the abdomen showed definite improvement in the dilated loops, but there was one large markedly dilated loop of small bowel, probably in the upper jejunum. The nonprotein nitrogen was 90 mg. 100 c.c. the chloride 108.4 milliequiv. per liter. The serum amylase was 1.5 units (normal). The van den Bergh reaction was too low to read. The prothrombin time was 25 seconds (normal, 20 seconds). In the bromsulfalein test 30 per cent of the dye was present in the thirty-minute specimen. The urinary sediment contained a rare coarsely granular cast, a rare red cell, 10 white cells, 5 epithelial cells, calcium oxalate crystals and rare crystals resembling sulfadiazine per highpower field.

On the seventh day after admission, the temperature rose to 101° and each evening it jumped to 103°F. The pulse ranged between 100 and 110. At this time the wound became infected with *Proteus vulgaris* and broke down. Because of intermittent abdominal distention, barium enema, gastrointestinal-series and intravenous pyelogram studies were made. The entire colon filled readily. The colon emptied completely and no organic lesion could be demonstrated. The small barium meal was negative. The barium mixture passed through the small bowel as far as the ileostomy opening in the

usual time without evidence of obstruction or dislocation. Palpation was unsatisfactory because of the patient's condition. The intravenous pyelogram demonstrated that the kidney outlines were normal in size, shape and position. At no time was the dye visible in the kidney pelvis. However, there was a moderate amount of dye in the bladder toward the end of the examination. The liver shadow was large. The spleen was not visible. Low in the pelvis on the left side were several dense shadows they probably represented barium in the diverticula of the sigmoid. The nonprotein nitrogen at this time was 28 mg. per 100 c.c. Owing to signs of pleural fluid, chest taps were performed through the ninth interspace on each side; 2 c.c. of what appeared to be thin blood was obtained from the right side, and 25 c.c. of similar fluid from the left.

Terminally the patient seemed slightly jaundiced. The serum bilirubin was 2.45 mg. per 100 c.c. direct, and 2.75 mg. indirect. The liver function test showed 50 per cent retention of the dye in the serum. The patient vomited small amounts of blood, and a small amount of blood drained from the enterostomy opening. The blood pressure dropped to 74 systolic, 40 diastolic, and the pulse rose to 120. In spite of supportive measures the patient died on the fortieth day after admission.

DR. T. H. BATE

The case under discussion today is that of a fifty-six year old white male who was admitted to the hospital because of abdominal pain, nausea and vomiting. The protocol is rather long, involving three pages. Numerous laboratory tests were done, numerous x-ray studies were made. In order not to review the entire history I will try to pick out the salient points upon which we might logically come to a conclusion, which of course we hope is the right diagnosis.

This patient had been bothered with colitis for about six months, supposedly proven with an x-ray. It is stated that he felt better in the day time than he did in the morning on arising. He had noticed an abundance of gas, but the stools were not described. Five days before admission he became constipated and was relieved by repeated enemas, passing a great deal of gas. Two days after this he started to vomit a thin yellow fluid and noticed an enormous distention of the upper abdomen. There is a twenty pound

weight loss and a definite history of alcohol. His admitting laboratory work showed an anemia, a leukocytosis, a 2 plus albumin and a 1 plus sugar in the urine, an increased serum of non-protein nitrogen of 122 mg. (25 to 32 being normal). The protein was depressed to 4.9. (normal being 6 to 8).

The x-ray studies revealed distention of the upper gastro-intestinal tract and a calcified mass over the 5th lumbar vertebra.

Numerous attempts to use the Miller-Abbott tube failed and an enterostomy was done. At this time, the hard mass described in the x-ray was felt to be calcified lymph nodes over the 4th lumbar vertebra. The omentum presented itself and areas were biopsied which showed fat necrosis. This might be the turning point of the whole case.

A few days later repeated physical examination revealed an enlarged liver. The NPN had fallen to 90. The protein had improved slightly coming up to 5.3. Blood sugar was 145 and serum amylase was normal. Apparently the House Staff at this time were considering pancreatic disease. Bromosulphathalein test showed a 30 per cent retention in thirty minutes, this is definitely increased, normal being about 10 per cent. The urine at this time showed a few hyaline casts.

On the seventh day the wound broke down and the patient became acutely ill. Barium enema, gastro-intestinal study and intravenous pyelograms were all described as normal. However, during the examination small diverticuli of the sigmoid were noted. Terminally, there was some fluid in the chest, a small amount described as thin and bloody. The patient was jaundiced terminally and died.

In reviewing the signs and symptoms on this case, several possibilities come to mind: *First*: Did the man have high intestinal obstruction. I do not think so, because first he passed a great deal of gas. This is characteristic of a chronic pancreatitis. The upper abdomen will distend enormously, vomiting is common and profuse, although usually thin in character, and the patient passes a great deal of gas. Whereas in high intestinal obstruction vomiting is prominent, it becomes progressively darker as the vomiting progresses. Pain is crampy and rhythmic, this patient did not have pain, and there is usually no expulsion of gas or feces. This is further borne out by the x-ray studies, namely, the nega-



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RESEARCH IN THE SERVICE OF MEDICINE **SEARLE**

tive gastro-intestinal series. The malfunctioning liver, with slight enlargement, will hardly explain the clinical picture given here. It has been shown on numerous occasions that pancreatic disease, of chronic nature is very often associated with a fatty degeneration and enlargement of the liver. It is stated by some authors that the enlargement of the liver and the fatty infiltration may be an attempt of the liver cells to supplement and aid in the digestive processes of the pancreas. Although most frequently associated with lesions of the pancreas, fat necrosis can occur under other circumstances. Traumatic fat necrosis has been found in the female breast, and occasionally it will develop in any fatty tissue subjected to trauma. In all instances, the lesion probably appears as the result of a breakdown of neutral fat by a lipase. Necrosis or injury to the tissue allows the fat to be released from cellular confines to meet the enzymes, whether it be liberated pancreatic enzyme, or a local ferment arising from the regions of traumatic necrosis. Fatty acid and glycerol are formed. Glycerol being water soluble is carried away, but the fatty acids may crystalize into irritating foreign bodies, or may unite with calcium ions into insoluble soap. Both products remain locally at the sight of injury. The calcium content of tissues subjected to fat necrosis is much higher than that of normal tissue. Perhaps the calcified masses described on x-ray and by the surgeon palpating through the incision for the enterostomy, may be the terminal results of previous fatty necrosis with the formation and union with calcium.

The symptom of abdominal pain, which was better in the daytime than at night, is also interesting and tends to lead to the diagnosis of pancreatic disease. DeCosta was the first to describe increased pain in the recumbent position, explaining that due to the retroperitoneal position of the Pancreas, the spine being hyper-extended is more apt to cause pain. As the patient is in the upright position he tends to stoop forward and in so doing relieves tension over the pancreas.

Carcinoma of the body and tail of the pancreas must also be thought of in this case. Duff points out that the clinical picture of cancer of the body and tail differs from that of cancer of the head in other respects than the presence or absence of jaundice. Spread in the cancer of the body and tail is a much more striking feature

than cancer in the head. This influences the signs and symptoms. Deep-seated gnawing pain is characteristic of cancer of the body, and is explained by extensive involvement of perineural lymph spaces, as the tumor is likely to be in direct contact celiac plexus. Ascites is common and is usually due to the implantation growths on the peritoneum or the involvement of the portal vein. The spleen may be enlarged owing to the pressure on the splenic vein, which lies in the groove in the body of the pancreas. Distant metastases, both by blood and lymph stream, are commoner than in cancer of the head.

CLINICAL FEATURES OF CHRONIC PANCREATITIS

In general, chronic pancreatitis has not been considered as a distinct pathologic entity, but has usually been regarded in conjunction with chronic cholecystitis, obstructive jaundice due to stone in the common bile duct, or carcinoma of the ampulla of Vater or of the head of the pancreas. Recently, Comfort, Gambill, and Baggenstoss have emphasized chronic pancreatitis unassociated with disease of the biliary or gastro-intestinal tract as "chronic relapsing pancreatitis."

Chronic pancreatitis may be defined as a disease characterized by recurrent attacks of pain in the upper abdomen, by disturbance of parenchymatous cell function, and by rather specific sequelae; a syndrome which may be limited to the pancreas alone or may be associated with disease of the biliary or gastro-intestinal tract. Attention has been devoted to the pathologic findings of marked interstitial fibrosis and residual cystic necroses of tissue as characteristic of chronic pancreatitis. The term "hydropancreatosis" has been used to denote the condition in which the duct system is dilated above a point of obstruction with extreme atrophy of the parenchyma.

Incidence and Exciting Factors

Chronic pancreatitis may begin in childhood or late in life, but usually starts most frequently in the third or fourth decade. It occurs more often among males than among females, the ratio being about 6:1 (Comfort, Gambill and Baggenstoss). Dietary indiscretions and alcohol appear to initiate the acute attacks. Size, weight, and obesity are probably not precipitating factors. Bustos (1945) stressed the possibility of

focal and systemic infection as a likely cause of chronic pancreatitis; however, Comfort et al. (1946) minimized infection as an etiologic hypothesis.

Symptoms and Physical Findings

Although there are no pathognomonic symptoms and signs of chronic pancreatitis the collective findings of pancreatic pain, dyspepsia, steatorrhea, diabetes, and occasionally a mass palpated in the epigastric region should direct attention toward this organ.

The pain in chronic pancreatitis usually starts abruptly, but is not always severe. It has been described as constant and burning, and usually, though not always, is provoked by food and alcohol, in contrast to the pain of chronic peptic ulcer, which usually is alleviated momentarily by the ingestion of food. The seizures of pain in chronic pancreatitis may continue over various periods of time, from a few days to as long as 10 to 20 years. The pain, usually steady, is frequently located in the epigastrium, although it is not uncommon in either of the upper abdominal quadrants. As in acute pancreatitis, pain in chronic pancreatitis may radiate transversely across the epigastric region, through to the back, or occasionally to the left costal angle.

The physical findings vary with the stage of the attack, which in many instances is so mild that there are no significant signs. Fever and leukocytosis, and in some cases even shock, are found. Usually there is some degree of muscle spasm in the upper abdomen. In a very thin patient with long-standing chronic pancreatitis an enlarged or cystic pancreas may be palpated as an indefinite mass. Jaundice occurs in almost half the cases with chronic pancreatitis.

Laboratory Features

Transient or persistent glycosuria represents a form of diabetes mellitus. Albuminuria is not uncommon. NPN may be elected.

Blood studies frequently show an anemia, and blood volume may fall below a normal level. Leukocytosis is a variable and an unimportant diagnostic feature. The presence of an elevated blood sugar and a diabetic type of glucose tolerance curve is extremely helpful from both a diagnostic and therapeutic point of view. The serum bilirubin determination may reveal subclinical or clinical jaundice. The blood serum amylase test may or may not be elevated, and this test is not nearly so valuable as in acute pancreatitis.

Hypocalcemia noted in acute pancreatitis is not present in chronic pancreatitis.

Examination of the stool is important, and the clinical picture of steatorrhea should warrant thorough investigation. Stools may vary from large, bulky, whitish, fatty ones to those of normal consistency. Microscopically, undigested starches (amylorrhea), proteins (azotorrhea), and fats (steatorrhea) may be found.

Roentgenologic studies of the gallbladder, stomach, duodenum, small intestine, and colon may demonstrate associated pathologic conditions. A roentgenogram of the pancreas will in about 50% percent of cases reveal calcification which represents a sequela of this disease. Many observers (Comfort et al.) believe the calcifications are the results rather than the cause of the disease.

DIAGNOSIS

Acute Exacerbation of Chronic Relapsing Pancreatitis.

DR. J. M. GREER

The high lights of the case are as follows:

A male patient fifty-six years old coming in with a history crampy abdominal pain, nausea and vomiting. The history reveals that about six months previously, the patient was awakened at night with crampy abdominal pain, nausea and at times vomiting. Five days before admission there were severe abdominal cramps and marked constipation. Three days later he began to vomit a thin fluid. There was no jaundice; nor tarry stools. He had lost about 20 pounds of weight in three months. He used to drink a large amount of rye whiskey to quiet his nerves but not in the last week.

The past and family history:—Not important.

Upon physical examination he looked ill, he was dehydrated, and his diaphragms were elevated, the chest movements limited but the heart and chest normal. T. P. R. was 99-94-21. The abdomen was enormously distended and peristalsis was weak. Blood Hb. 10.5 gm. reds 3 M. whites 16,000. Urine showed 2 plus alb. low specific gravity and green sugar test. The serum NPN was 122 mgm to 100 cc. (normal is 25-35) This went down to 90 and then 28 after enterostomy and treatment.

X-ray showed dilated stomach and small intestine and some large dilated loops of small intestine, colon was not dilated.

Maybe the most significant thing was a large

area of calcification overlying the area of the fifth lumbar vertebra.

A laparotomy was done under local anesthesia, going in on the left side. It seems to me that this was a peculiar way to do a laparotomy but they do doubt had their reasons. They probably only intended to pick up a loop of bowel for enterostomy and decompression as they were unable to pass a Miller-Abbott tube. At any rate the calcified mass was palpated and an enterostomy done, and some necrosis of the omentum was found.

The patient improved for a few days and the NPN went down. However, he developed liver and chest complications and a small amount of bloody fluid was aspirated from the pleural cavity and he went down hill and died on the fortieth hospital day, in spite of voluminous blood chemistry and x-ray studies and efficient treatment.

Now let us go over the case more carefully:

The above outline of history and symptomatology as well as physical examination and laboratory work point toward some pathology in the abdomen, and involving the abdominal organs, and at least manifest by symptoms involving the intestinal tract. The extreme abdominal cramps and constipation strongly suggest mechanical obstruction, but when they listened the peristalsis was weak. Was that because of the length of time or was it a mechanical obstruction? Is there anything in the physical findings that will help us? We know that there is a mass in the abdomen because it has been x-rayed and has been palpated when laparotomy was done.

This Mass:—If we knew all about it we would probably have the diagnosis of our case or would we? This mass in the abdomen in the area of the 5th lumbar vertebrae, this mass, this stony hard mass that was palpated when laparotomy was done, this mass that is calcified and shows by x-ray. I take it that this mass is hard and fixed, and in the region of the last vertebrae, and probably projected forward in the retroperitoneal area and could have interfered with the retroperitoneal blood supply. Could it be the cause of an intestinal obstruction? It is possible that it or the inflammation around it could well be. We also have to think of a mesenteric thrombosis. Is this mass inflammatory or in the nature of a new growth? If it is a new growth is it benign or malignant? As to retroperitoneal tumors, these tumors may occur anywhere in the

retroperitoneal area. They may be malignant or benign and are lipomata, fibromata, myoma, chondroma, neuroma, sarcoma, and lymphadenoma, and all varieties of cysts.

We should probably take this mass for what the attendants thought it was, namely, a calcified mass of lymph nodes, and dismiss the idea of a retroperitoneal tumor, as we have very few other symptoms or signs to support it.

From the physical findings of the abdomen;—distention, large dilated loops, fluid, vomiting, with temperature and leucocytosis we must assume that he had some peritonitis and no doubt the attendants thought so too as he was given sulfadiazine intravenously. Also after many unsuccessful attempts at passing a Miller Abbott tube the abdomen was opened under local anesthesia and an enterostomy was done. Was this done because of a mechanical ileus or lleus following peritonitis? Probably the latter. The mass was palpated and necrotic masses of omentum found.

The numerous gray areas of fat necrosis on the omentum are to me significant, and make it necessary to investigate the possibility of pancreatic involvement, as a pancreatitis is the most likely thing that would cause such necrosis. This is probably the key to the diagnosis as it is a physical sign of irritation from pancreatic fluid which means pancreatitis.

We usually think of acute pancreatitis as being a sudden overwhelming disease; however this is a question of degree and there are less severe cases, and they do not all manifest the same degree of severe upper abdominal pain and shock. In the severe gangrenous and hemorrhagic forms the mortality is about 80%, and this goes on down to 10% depending upon the degree of involvement. As we know these pancreatitides are brought on by blocking of the ducts or interference with the blood supply, from infection and thrombosis. This could well be the cause in this case.

The patient improved somewhat after laparotomy and enterostomy but on the seventh day started to have a rise in temperature and pulse and went down hill from then on.

Gastro-intestinal studies and IV pyelograms were done which probably did the patient very little good as he must have been quite ill with temperature up to 103° and pulse 110, and the protocol states that palpation was unsatisfactory because of the patients condition.

We are told that the barium enema showed that the colon emptied completely and later we are told that there were several dense shadows in the left pelvis as evidence of diverticulum of the sigmoid. Probably they do not consider the sigmoid as a part of the colon. The patient may have had some trouble with diverticulitis, which may have been a factor in the cause of the calcareous lymph nodes, and this as an etiological basis of the pancreatitis and the other abdominal pathology.

The signs of the pleural fluid and bloody chest taps developed during the last few days and are a little hard to explain except that there had developed an associated hepatitis and liver congestion which could have accounted for this finding. Also if he had developed a retroperitoneal or mesenteric thrombosis the bloody fluid in the chest could have come from this. Probably the most likely thing is a necrotizing pancreatitis and as this is a retroperitoneal organ the bloody fluid came from this.

In Summary:—

A male patient fifty-six years of age with a six months history of crampy abdominal pains, bloating, eructations, belching and much gas, indicating, at least, partial intestinal obstruction—more manifest five days before entry by extreme cramping and constipation. At the time of entering the hospital very ill with clinical peritonitis, with ileus intestinal obstruction which was only relieved by laparotomy and enterostomy, at which time omental necrosis was found. Later developing hepatitis, liver congestion and bloody fluid in the chest, ending in death on the fortieth day.

These findings, history and progress, indicate to me a diagnosis of chronic pancreatitis, later developing into an acute pancreatitis with peritonitis, with at least partial obstruction for which enterostomy was done. Liver and chest complications developed which added to the cause of his death.

One would expect to find the pathological changes in the various organs of this clinical picture.

My diagnosis would then be:

Pancreatitis, subacute and gradually developing into a necrosis of the pancreas with bloody fluid in the peritoneum and chest cavity. All this was of sufficient degree to cause death.

DIFFERENTIAL DIAGNOSIS

Dr. Arthur W. Allen: Are the original calcified areas still present in the later x-ray films?

Dr. George W. Holmes: Yes.

Dr. Allen: According to the history, this man should have had a lesion easily demonstrable by x-ray, and it is a great disappointment to me that the x-ray studies throw so little light on the problem. We have a history that is perfectly consistent with a slowly developing lesion of the gastrointestinal tract that finally produced complete obstruction. This, however, probably is not the case since I am sure that under such circumstances the x-ray studies made after the sixth day of hospitalization would have been more conclusive than they appear to be.

Starting back with the fistula operation fifteen years before admission, a fistula of sufficient dimensions to require destruction of the sphincter makes one think of the possibility of tuberculosis. The calcified areas, which I assume represent healed tuberculous nodules in the mesentery of the ileum may not have had any bearing on such a possibility. They were probably due to a healed bovine tuberculosis that he developed in childhood because of drinking raw milk. Although these calcified nodes do cause symptoms in certain cases, they rarely produce acute obstruction. Usually they are symptomless and very little attention is paid to them by clinicians, sometimes very much to the detriment of the patient.

The present illness seems to have started about six months prior to admission when he began to have crampy abdominal pain, which was usually followed by nausea and at times by vomiting. This was worse at night when he was recumbent and better in the daytime when he was up and moving around. Although we have a note a little farther along saying that for many weeks prior to admission he was in the habit of drinking a pint of rye daily, it does not state whether this habit preceded the beginning of his difficulty six months previously, and I have a feeling that that is irrelevant. He had a sufficient amount of trouble five months prior to admission so that his physician urged him to have a barium enema and x-ray studies. The x-ray studies revealed "colitis," which is a vague and indefinite term and means very little. However, at that time they probably ruled out a demonstrable growth in the intestine, and his physician was apparently satisfied to let the matter of crampy pain rest

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at the moment and possibly blamed this discomfort on the patient's alcoholic intake. He really developed a good deal of change in his bowel habits about a month prior to admission. He had previously had loose bowel movements, which is rather an unfortunate complication for a man who has a sphincter that is not functioning. However, this shifted over a month prior to admission to constipation, at that time he was aware of a great deal of gas in his bowels. Five days before admission the patient became very constipated, and I assume that he failed to have any bowel movement, that he had extreme abdominal pain and that the abdomen became distended. He was brought in here in a state of dehydration and was obviously in a very precarious condition.

At the time of entry the laboratory evidence, as represented by a high nonprotein nitrogen, a low blood chlorides and a low protein, confirmed the story that he had been unable to take any food or fluid for five days. He had also a certain amount of anemia—a red-cell count of 3,000,000. He had some leukocytosis, which may or may not have been of any significance since he must have had some hemoconcentration at the time the count was made. The red herring about the green sugar test is cleared up by the negative test later. The fact that the Miller-Abbott tube failed to pass the pylorus was undoubtedly a disappointment to those who treated him, particularly since every effort had probably been made to get this tube through the pylorus. I wish to call attention at this time to a very excellent description by Dr. Abbott, of how these tubes may be passed with a fine wire stylet. This wire can be obtained from sporting-goods houses since it is made for fishing leaders. The type of material that can be brought in Boston is not exactly the size that Dr. Abbott recommends but it is effective, and by the simple technic that he describes, in approximately 24 out of 25 cases one can be sure of getting the tube passed effectively.

Dr. Clifford C. Franseen: It was used in this case.

Dr. Allen: Yes, I assumed it was; but I am sure that not enough publicity has been given to the technic. That is why I bring it up here.

The exploratory laparotomy interests me. Why did the surgeon choose the left side rather than the right? Perhaps the patient was a little more distended there, or the surgeon may have thought

that he could feel a lower segment of ileum on the left. Possibly in the flat plate there was a loop presenting on the left, which gave him a lead to enter on that side. The two-finger exploration coming in contact with a hard mass, which was assumed to be this calcified mass of lymph nodes, is interesting and it may be that it finally turned out to be something else. Also the question of fat necrosis on a little tag of omentum interests me a good deal because the fluid that came from the abdomen was straw colored. In fat necrosis associated with acute pancreatitis the fluid is rarely straw colored but is blood tinged or the color of prune juice. The fact that the biopsy of the omentum showed fat necrosis is of considerable interest in the light of the type of fluid. Fat necrosis can occur without pancreatitis, but it occurs usually after trauma in the breast of subcutaneous tissues.

The man improved following ileostomy, which shows that a low loop of bowel was encountered, and undoubtedly he got a great deal of benefit not only from the ileostomy but also from the Miller-Abbott tube, which apparently remained in the stomach. They were able to feel his liver edge on the sixth hospital day. It could not be felt on admission because of the distention. It was three fingerbreadths below the costal margin and seemed rough and uneven to touch. Then the patient began to have periods of distention again but was able to withstand a gastrointestinal series, a barium enema and an intravenous pyelogram. His chemical balance had improved considerably by the sixth day, and up to that time he had had no evidence of jaundice. The prothrombin time was only slightly elevated. Although the record does not say so, the probabilities are that he had been given synthetic Vitamin K prophylactically. He certainly had a good dose of sulfadiazine, which raised the blood level to 17.6 mg. per 100 cc. Although it seems from the record that this drug was not started until the third day after admission, it is likely that it was started before that time. However, this did not prevent the patient from having a certain amount of infection in the wound. Nearly all enterostomy wounds become infected, and this wound behaved about as one would expect it to.

Interestingly enough the patient developed a high temperature on the seventh day; it went up to 103°F. each evening, and the pulse rose. That could have caused the elevation of the

diaphragm, which was not reduced by the relief of the distention? Then the question comes up. What was the thin bloody fluid in the chest? Since so little was withdrawn the probability is that there was not so much fluid there as they had suspected.

Then there comes a big hiatus in the history. We have a good deal of detail up to the seventh day, and then a very brief description of the last few days of the patient's illness. Terminally, he became jaundiced, and the liver-function test showed 50 per cent retention; he vomited small amounts of blood, and a small amount of blood drained from the enterostomy opening. He died on the fortieth day after admission, which is exactly the right time for a patient to die with necrotizing pancreatitis. The patient that almost but does not quite survive pancreatitis is very apt to live just about six weeks.

This man's story is very confusing and it brings up a lot of interesting points. One may hazard a good many guesses about where the underlying pathologic process really was but the chance of being right, so far as I am concerned, is very remote. The patient could perfectly well have had an ileus without having either an intrinsic or extrinsic lesion in the bowel; that is, the ileus could have been on the basis of gastritis and alcoholism. However, he had lost 20 pounds in weight. This man was developing a disease that manifested itself as an acute picture when he came in but actually was an end result of something that had been going on for a period of nearly half a year, possibly longer. It is conceivable that he could have had a reactivation of his mesenteric adenitis. When I saw the first film and read the story, it occurred to me that possibly this was going to turn out to be a gallstone ileus, but I now believe that the film does not have the appearance of a gallstone in a loop of small bowel. One might consider that this was really just cirrhosis of the liver, and pin everything on that as a diagnosis, but there is very little evidence of that.

The palpation of the liver, the size of the liver, the ileus and so forth, are compatible but I think such a diagnosis is rather farfetched. The patient could have had, I suppose, some chronic situation in the pancreas that might have led up to an acute episode of this sort, but it seems rather unlikely. It is certainly not the usual history for a man to have a warning six

months prior to the time he comes down with pancreatitis, which usually comes out of a clear sky without any long prodromal history. One has to think of tuberculosis, as I mentioned earlier in the discussion, because there is some evidence of certain types of tuberculosis in his past history. I am not sure about the chest; I should suppose that Dr. Holmes would say it was clear so far as any chest lesion is concerned.

That brings us down to the possibility of a lesion in the small intestine of a carcinomatous nature, which might conceivably have been overlooked. It is possible that such a lesion in the small bowel might have been between the point of ileostomy and the portion of the ileum filled from the barium enema. I think that is the most likely diagnosis. The reason I think so is that it is the one area that could not be definitely ruled out by the surgeon and that could not be studied by the x-ray man, using contrast mediums. The next best possibility is some extrinsic neoplasm secondarily involving the bowel. In this instance I assume that the liver was full of tumor and that is what was the matter with the liver, not cirrhosis.

Dr. Holmes: May I add a few points? In these films it does not look as if the liver conforms to the clinic interpretation. It is a little large but not abnormal in shape. The hepatic flexure is not displaced downward. I wonder if you put enough weight on the fluid in the left pleural space. There was some fluid there earlier, and later a considerable amount.

Dr. Allen: The patient could have had carcinoma involving the diaphragm, or a primary lesion of the lung, if you choose. I am not worried about the chest picture. In carcinoma of the abdomen one often sees fluid in the chest, many times because the diaphragm is studded with carcinoma.

Dr. Franseen: The site of the ileostomy was chosen because at the time of the flat film the point of obstruction appeared to be in the ileocecal region and we wanted to reserve the right lower quadrant for the second operation.

Dr. Dwight L. Siscoe: I followed this patient very closely outside the hospital. Dr. Allen included all diagnoses that we were interested in and considered some more too. There were a few points that Dr. Allen questioned. One was the alcohol. The alcohol made a much greater impression on our minds than the record here would suggest. The roentgenologist who

first examined him was greatly impressed by the gastritis and the amount of alcohol consumed. In fact we received word that he had been using a quart a day instead of a pint. So the possibility of cirrhosis was very much in our minds. During the last few days of his life the patient ran a steady downhill course, and a few days before death one observer believed that he felt a mass in the right lower quadrant.

Dr. Franseen: The patient was scheduled for operation, but that morning had a large hemorrhage and the operation was called off. That was twenty-four hours before death.

CLINICAL DIAGNOSIS

Carcinoma of stomach?

Portal cirrhosis?

DR. ALLEN'S DIAGNOSIS

Carcinomatosis, involving the lower ileum.

ANATOMICAL DIAGNOSIS

Pancreatitis, hemorrhagic, subacute.

Fat necrosis, extensive.

Rupture of splenic artery and vein.

Erosion into duodenum, with massive gastrointestinal hemorrhage.

Chronic cholecystitis.

Cholelithiasis, with stone in ampulla of Vater.

Tuberculous mesenteric adenitis, healed.

Arteriosclerosis, moderate: aortic, coronary and renal.

PATHOLOGICAL DISCUSSION

Dr. Tracy B. Mallory: An autopsy innumerable foci of fat necrosis covered the peritoneal surfaces from the bottom of the pelvis to the inferior surface of the diaphragm. The entire pancreas had been destroyed, and the retroperitoneal tissues of the upper portion of the abdominal cavity were occupied by a huge blood-filled cavity with shaggy, necrotic walls. Into this cavity dangled the ends of the splenic vein and artery, neither of which was thrombosed. A spontaneous rupture had occurred into the posterior wall of the third portion of the duodenum, so the terminal event was evidently hemorrhage from the splenic vessels into the cavity and hence into the duodenum, filling the gastrointestinal tract with blood. It was interesting that both pleural cavities contained small amounts of clear strawcolored fluid so the supposed chest tap must have penetrated into the retroperitoneal cavity. The extremely high diaphragm made this readily possible. The liver was at the upper limit of normal in size, weighing 1800 gm., and was not nodular or cir-

hotic. It did show extensive acute central necrosis, which accounts for the terminal liver insufficiency.

This man had the classic setup for acute pancreatitis. There was a severe chronic cholecystitis with innumerable small stones. The prodromal symptoms that led Dr. Allen to trace the onset of his illness back at least six months may well, in retrospect, have been due to his gallbladder. There was likewise a small stone in the common duct partially imbedded in the mouth of the duct of Wirsung. There was thus a real possibility of reflux of bile into the pancreatic duct. It must be admitted, of course, that few cases of pancreatitis show a calculus in the appropriate location.

Dr. Allen: The straw-colored fluid, five days after the pancreatitis started, is the thing that bothered me. Do you believe that that is usual? We frequently do a paracentesis to make a differential diagnosis between pancreatitis and perforated ulcer, and things of that sort, and we rely on the character of the fluid to guide us.

Dr. Mallory: I should consider clear yellow fluid unusual too.

Dr. Allen: The serum amylase determination, so far as I could tell from the record, was not done till the fifth or sixth day, so that it had to be thrown out as a guide. If that had been done the first day I think it would have had more significance.

Dr. Joseph C. Aub: Why does a patient with pancreatitis die on the fortieth day?

Dr. Allen: It takes just about that long for the pancreas to become completely necrotic and erode a big vessel, usually the splenic artery.

Dr. Siscoe: I am sorry Dr. McKittrick is not here to discuss this case, since he held out for the diagnosis of pancreatitis almost from the start. He believed that the intra-abdominal fat necrosis could be explained in no other way.

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TOPICS OF CURRENT MEDICAL INTEREST

REPORT OF THE DELEGATE

Clinical Session, American Medical Association

Cleveland, Ohio, Dec. 5-8, 1950

Preceding the opening of the Clinical Session, and the meetings of the House of Delegates, the Third National Medical Public Relations Conference was held. Emphasis was placed upon several fundamentals which constitute a well rounded program of public relations. It was emphasized that the *Individual physician* was the base upon which all good public relations could build a pyramid extending up thru the County, State and National Organizations. From this Base, the Individual Physician, thru his education and practise of good public relations, emanate all other plans and procedures, ideas and ideals, so that collectively, thru the County Medical Society, a program of good public relations can be promoted in various communities, the work of the State Society on a more extensive basis; and the overall program aimed at a national audience through the educational and public relations program of the A.M.A. Good public relations must stress the individual physician-patient relationship as the keystone to a successful program. Each individual and county medical society should ask themselves the following questions: Is 24 hour emergency service maintained in your community? Are you willing to care for patients when they call at 2:00 A.M.? Is there emergency telephone service to the hospitals. Are the charges for services in line with an average charged by physicians in your community? Is there an attempt to maintain an average and fair fee schedule? Are charges for services explained first, instead of waiting for a patient to criticize the fee as unfair or exorbitant? Are these problems discussed in county medical society activities with new members of your Society? Or to acquaint new members with local customs? Does your county medical society insist that each member read and become acquainted with the "Principles of Medical Ethics," and your Constitution and By-Laws? Does your county society have a grievance committee that really functions? Do you have a good press relations committee to iron out difficulties in public relations? Do all the people in

your Community receive good medical care? If not, what can be done to facilitate this care? Many other questions could be asked.

If then, good public relations begin at home, what does your reception room look like, and what have you done today, if anything, to break faith with your professional endeavors, and cause one break in the chain of Good Public Relations?

Another important event at the Clinical Session was the reading before the House of Delegates, and all others assembled, of a paper prepared by William L. Hutcheson, President, United Brotherhood of Carpenters and Joiners, and Vice-President of the American Federation of Labor. This paper represented the first definite indication that a large segment of organized labor, thru its President, had joined hands in its struggle to defeat compulsory health insurance in this country. The address was broadcast nation-wide over the A.B.C. network. Mr. Hutcheson stated in his paper: "I am against socialized medicine. So is the organization which I have the honor of heading." (700,000). His concluding paragraph—Quote—"I have always respected the medical profession for the fine contribution American Medicine has made to human Welfare. As I watched your battle against regimentation during the past two years, I have added to that respect. The physicians of this country have shown that they are willing to fight for their convictions. I salute you today not only as doctors but as crusading citizens as well. We in the labor movement have our own cross of regimentation to bear. The fight you are making is part of the same war. It is a war against concentration of authority in a few hands in Washington. As a veteran of forty years in the labor movement, I know what it is to fight for human rights. I am happy to take my stand beside you." Unquote.

At this session of the House, through a public announcement by the Chairman of the Board of Trustees, the A.M.A. appropriated a half million dollars as a nucleus of a fund to be raised for the aid of medical schools. That fund, with-

in a few hours after the Board's decision had been announced, had been swelled by thousands of dollars spontaneously pledged by individuals and from other sources. It was the A.M.A.'s evidence of concrete action in its opposition to Federal Subsidies for the medical schools as offered in bills introduced in the last Congress. It is hoped that this fund will be augmented and will act as a "stimulus to other professions, industries, businesses, labor groups and private donors to contribute to this very important cause of protecting and advancing the interests of medical education and public health."

And now for a discussion of some of the other subjects before the House of Delegates.

1. The Board of Trustees asked the conference if it desired to continue the Clinical Sessions. The Reference Committee called attention to Article 2 of the Constitution which says. "The objects of the Association are to promote the science and art of medicine and the betterment of public health." It recommended continuation of the Clinical Sessions, and the House adopted its report. The House selected St. Louis as the site for the 1953 mid-winter session. Next year session will be held in Houston, Texas, and Denver in 1952.

2. A Resolution was introduced into the House relating to the problems of Alcoholism. It was adopted in substance, but referred to the Committee on Chronic Diseases, instead of creating a new committee of the House.

3. The A.M.A. Committee on Blood Banks, in its report to the Board and House, emphasized that the national emergency blood program "is and must continue to be a three pronged activity, each part of which must be developed to keep the whole program in balance. The three part are: a. furnishing of whole blood and plasma to the Armed Services. b. maintenance of supplies of blood and plasma for normal civilian requirement; c. the development of dispersed reserve supplies of equipment for collecting blood and dispersed reserve supplies of blood plasma for civilian defense. The Committee urged each state medical society to establish a state committee on blood banks whose function it would be to correlate the elements of the emergency blood program in its state and to see that blood procured is properly channeled. These committees should include representation from hospitals, blood banks, and Red Cross. A state committee could function so that there

would be no duplication of effort, overlapping of blood procurement by different organizations, and avoid the confusion resulting therefrom.

4. Facts about the A.M.A. dues. Dues for 1951.

Fellowship dues for 1951 are \$5.00; and are exclusive of \$25.00 for membership dues.

A.M.A. dues are payable through the component county medical society or the constituent state or territorial medical association, depending upon the method adopted locally.

Fellowship dues are payable directly to the headquarters of the A.M.A. on receipt of a bill for such dues.

A dues paying, acting member is eligible for Fellowship and may request such status by direct application to the Secretary of the A.M.A. Applications for Fellowship are subject to approval by the Judicial Council.

An active member of the A.M.A. may be excused from the payment of membership dues when it is deemed advisable by the Board of Trustees, provided that he is excused from payment of full dues by his component society and state association. The following may be excused: (a) members for whom the payment of dues would constitute a financial hardship, as determined by their local medical society; (b) members in actual training for not more than five years after graduation from medical school, and (c) members who have retired from active practice. "Honorary" members, who are also active members of their societies are not excused from payment of dues, even though they do not pay dues to their local societies.

Membership dues in the A.M.A. includes a subscription to the Journal of the A.M.A. Active members who are excused from payment of dues will not receive the Journal except upon payment of the regular subscription rate of \$15.00 per year.

An active members is delinquent if his dues are not paid of Dec. 31 of the year for which dues are prescribed, and shall forfeit his active membership in the A.M.A. if he fails to pay the delinquent dues within thirty days after a notice of his delinquency has been mailed by the Secretary of the A.M.A. to his last known address. A member so dropped for non-payment of dues cannot be reinstated until such indebtedness has been discharged.

The apportionment of delegates from each constituent association shall be one delegate for

each one thousand (1,000) or fraction thereof, dues paying active members of the A.M.A. as recorded in the office of the A.M.A. Secretary on Dec. 1 of each year.

5. *Council on National Emergency Medical Service:*

The report of the Reference Committee on the Council on National Emergency Medical Service should be of interest. This Council has been active with other groups in working out details necessary for an adequate Civil Defense program, and in the procurement of medical officers for the Armed Services. American medicine must exert a forceful, dynamic leadership in the civil defense program of the nation at national, state and local levels, and following recommendations were made and adopted.

a. that each state seek adequate representation on civil defense advisory committees at all levels of government.

b. that the A.M.A. request appointment of an advisory committee of civilian physicians in the new Civil Defense Administration.

c. that a copy of the report of the Council on National Emergency Medical Service be sent to all secretaries of state and territorial associations, and State Chairman of Emergency Medical Service Committees.

d. That the Council on National Emergency Medical Service and the Committee on Blood Banks have some appropriate space in the A.M.A. Journal so that information regarding actions and recommendations of these committees can be brought to the attention of our members.

e. That the State Committees on Emergency Medical Service complete their programs without delay if they have not already done so, and stress the importance of their work in the overall civil defense program.

6. *Hospital Standardization:*

The Board of Trustees has given serious attention to the acute and ticklish problem of hospital standardization, which arose last June after the American College of Surgeons relinquished this task. At joint meetings with representatives with other interested groups, it was suggested that a joint commission be established representing the four major groups, namely the A.H.A., A. C. of S., the A. C. of P. and the A.M.A. A rough draft of a proposed constitution and by-laws has now been prepared by a joint

committee of these groups, negotiations are in progress, and much advancement has been made. Every effort will be made to reach satisfactory arrangements.

7. *Resolution on Council on Federal Medical Services*

This resolution was adopted after study by the Board of Trustees and the Council on Medical Service. The Council's Committee on Medical Care of Veterans will be changed to the Committee on Federal Medical Services. The Council on Medical Service will enlarge this Committee to meet the requirements of the specific functions enumerated in the resolution; that is,

a. Advising the Board of Trustees on all aspects of the several forms of federally supplied medical care either now or to be established.

b. Serving the Board of Trustees and the Association in conference with and in representations to both non-governmental and governmental agencies interested in the several forms of federally supplied medical care, and

c. Advising the House of Delegates at each of its regular and special sessions of any policy or change in policy of the Association relating to the several forms of federally supplied medical care which may require its consideration and action.

8. The House of Delegates adopted a resolution at this session instructing the Board of Trustees to seek amendment to the Federal Law on Workman's Compensation to the effect that all covered federal employees be granted *free choice of physician* for injuries sustained in line of duty.

9. Upon recommendation of the Council on Scientific Assembly, the House adopted a resolution creating a new Scientific Section of the A.M.A. to be known as the Section on Military Medicine.

10. *Constitution and By-Laws of the A.M.A.*

The Interim Committee on Constitution and By-Laws made a lengthy report to the House of Delegates, suggesting many changes which were accepted by the house upon recommendation of the Reference Committee and which will be acted upon formally at the next meeting in June. The House also adopted the suggestion that a permanent Committee on Constitution and By-Laws be created, which would serve as a fact finding and advisory body to study and

report on matters pertaining to the Constitution and By-Laws. This Interim committee also studied a resolution which would provide for one general classification of members in the A.M.A. The Committee members were unanimously opposed to this amendment which would change the present distinction between a Member and a Fellow. The recommendation was supported by the House.

11. *State Cash Sickness Disability Benefits (Temporary).*

Pending establishment of an over-all policy reflecting the attitude of organized medicine toward these programs as adopted in a few states and contemplated in many others, the following four minimum safeguards were adopted, to act as guide in this field of study on the part of physicians: (1) In the case of possible legislative enactment the prevention of abuse and extension of the program into allied fields. (2) Limitation of benefits to cash indemnity only. (3) Limitation of physicians duty to reports on diagnosis, prognosis and ability to work, and (4) Provision of medical supervision or review for maintenance of suitable standards of reporting.

This subject has been under careful study by the Council on Medical Service during the past year, but a complete digest of the material which has been assembled by the Council Staff has not yet been completed, so that it was thought best not to attempt the formation of a complete policy respecting the best methods of providing such coverage under these State Laws.

12. *Resolution on Medical and Hospital Care of Veterans with Non-Service Connected Disabilities*

Resolutions dealing with this subject were received from Tennessee supported by Michigan, Wisconsin and Louisiana, and another one from Pennsylvania. The House adopted the recommended proposals of the Reference Committee on Insurance and Medical Service wherein the Board of Trustees was authorized to permit the Committee on Legislation of the A.M.A. to offer its services to the government authorities of the Veterans Administration, or to the Congress, in seeking either administrative or legislative support for the following three principles: (1) The best possible care of all veterans with service-connected disabilities in Veterans Administration facilities; (2) the best possible care of veterans with non-service connected disabilities

who need financial support, and (3) veterans with non-service connected disabilities who are able to do so should provide their own care.

This Clinical Session of the A.M.A., aside from the scientific program for general practitioners, and the meeting of the House of Delegates, was highlighted by the two day Public Relations Program and the afternoon program developed by the National Educational Campaign Committee together with Whitaker and Baxter, wherein the accomplishments of this department of the A.M.A. were reviewed. These meetings were attended in full by your delegate and by the Executive Secretary of our State Association, Mr. Robert Carpenter. The weather in Cleveland was usual for this time of year, snow, cold, rain, smoke, smog, sleet and fog. It was nice seeing the sun again somewhere on the way home, where we were re-routed with several prolonged stop-overs due to inclement weather throughout the midwest.

Respectfully submitted

Jesse D. Hamer, M.D., Delegate



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By GUILLERMO OSLER, M.D.

Bits and bites of the **RELATIONSHIP BETWEEN MEDICINE AND THE LAW** are contained in a symposium reported by the *Annals of Western Medicine and Surgery* (published by the Los Angeles County Medical Ass'n.) . . . The symposium included several California experts, visiting-professors Roscoe Pound, Ford of Harvard, Gradwohl of St. Louis, Moritz of Western Reserve, etc. . . . It seems worth more than the 25 cents which the journal costs.

A new **DEODORANT** against hospital odors is described by Dr. Philip Brown of Detroit, in 'The Journal' of Michigan . . . The material is odorless, is a quaternary ammonium compound, can be used in toilets, psychiatric wards, and even (safely) in solution for spraying wounds with a fetid odor. It is bacteriostatic, with a phenol coefficient of 200 to 400 against various staph and strep strains. . . . It is made by the Associated Laboratories, Inc., of Ann Arbor, and could be worth a trial.

The **MORTALITY FROM ACUTE APPENDICITIS** is decreasing, as one might hope. . . . Hawk, Becker, and Lehman of the University of Virginia Hospital have compared 1,069 cases from the 1933 to 1937 era with 1,003 cases from 1943 to 1948. The mortality from the earlier period was 3.27%; and that of the recent period was 0.8%. . . . The decrease was ascribed in part to chemotherapy and antibiotic agents, especially streptomycin. . . . The data suggest that early operation, under modern conditions, has no advantage over conservative therapy for localized appendiceal peritonitis, but that it may have for diffuse peritonitis.

Appendicitis, incidentally, has one odd cause in Detroit. Raftery, et al., have examined specimens from 2,135 cases, and found **HISTOPLASMOSIS** to be the cause in 5 per cent.

Number Five on our list of methods for converting **SALT SEA-WATER TO FRESH WATER** has recently been described. It will interest a man in a boat, but not the population of arid Arizona and California areas. . . . Three-fourths of a pound of powdered silver fluorosilicate is added to one gallon of water. The solid salts are allowed to settle, and are then removed. The magnesium and the fluorosilicates are brought down by the addition of half an ounce of lime. The clear water is then potable. . . . All rights have been assigned to the U. S. Government.

A series of papers on **PEPTIC ULCER** in the *Annals of Surgery* has demonstrated several points. . . . Moore, et al., of Boston believe that a frac-

tion of ulcer patients (called 'progressive virulent ulcer disease') do badly with conservative therapy, and should have definitive surgery as soon as diagnosed. . . . Hinton of New York believes that a chronic penetrating duodenal ulcer should be removed in toto, to prevent leakages after surgery. . . . Dragstedt and colleagues report the fasting nocturnal gastric secretion to be 3 to 4 times normal in a patient with duodenal ulcer, and to be reduced to one-fifth after complete vagotomy. The 'nervous phase' accounts for about 80% of the gastric secretion, the 'antrum phase' 15%, and the 'intestinal phase' 5%. . . . Glenn of New York warns that secondary operations for ulcer succeed in only 50% of the cases, the mortality rate is high, but the procedure need be rare if the first choice surgery was well and wisely done. . . . The management of massive bleeding from a peptic ulcer is still controversial. Patterson of New York considers the problem a surgical one and resects one out of every three with a 6% mortality. Cole of Chicago operates on some of the bleeders, transfuses them all (as he says everyone does). . . . Paine, and Witebski, say that patients who are Rh negative and have never been transfused may receive Rh positive blood for 72 hours without hazard. . . . Bowers and Rossett of Memphis carried all but one of 150 cases through the emergency without surgery, and gastric resection was done later on 24 of the patients. The overall mortality was 1.3%. . . . The medical therapy consisted of absolute bed-rest and quiet; no tobacco; sedation, with barbiturates rather than opiates; psychotherapy; a Meulengracht regimen, but with feedings every 2 hours night as well as day, with a bland protein diet; neutralizing powders in milk for night feeding; and alkalis and antispasmodic drugs if vomiting is present.

What a change just a few hundred years can make. 'Drug Topics' tells of the superior healing qualities which **SINGLE, MALE PHYSICIANS** were supposed to possess in the 15th century. Today an unmarried GP, or especially an **OB-GYN** man, would have about as much chance of making a living as a witch-doctor. Maybe less.

Arizona is extremely lucky to have the basic work which was done on **FLUORINE** in water by the Smiths of the University of Arizona. They have mapped the status of water supplies all over the state, and the dentists and **USPHS** have since carried on with the clinical usage. . . . The contrast with other states is sharp. California is checking teeth and water where indicated and when forced to, far in arrears of the Arizona knowledge, and even farther from the fluorinization work of several mid-western states. . . . Viva Smiths!

Surgical treatment of bronchial asthma was discussed at length by the American Ass'n. for Thoracic Surgery in the spring of 1950. The results were not as promising as had previously been hoped. . . . The following comments were notable,—The treatment is 'empirical'. Denervation of the lung, or 'plexectomy' should be bilateral. The results are better when denervation is combined with resection of infected lung, or 'trigger' areas. The average percentage of severely asthmatic patients relieved is less than 50%, especially at a late date. Vagal section is not wise. Pioneers in the therapy are not enthusiastic, but urge work on the method. Cortisone, a heretical medical method, was mentioned as a further reason for surgical caution by Drs. H. J. Stanford of Tucson and Emile Holman of San Francisco.

Now and then the thought occurs "Why hasn't science replaced the old fashioned sources of certain chemicals? Why do they still extract Vitamin A from fish livers?" . . . It has, and they do not. . . . Reliable synthetic METHODS FOR PRODUCING VITAMIN A have recently put the shark-fishing industry out of business in many areas. The shark livers at Salerno, Florida were once worth \$500,000 annually, now almost nothing.

Medical science edges in on the disease which do not yet perfectly respond to treatment by endlessly using and combining new drugs and methods. . . . Nitrogen mustard has been of value for lymphomas, but has damaged the hematopoietic system too much to be of value against neoplasms. Regional radiation has been of some value because of its selectiveness. . . . Klopp and his colleagues in Washington, D. C. have combined the best part of the two methods when they discovered that NITROGEN MUSTARD SEEMS HELPFUL WHEN INJECTED INTRA-ARTERIALY, INTO A PART. They report the method in Annals of Surgery, and someone will soon find a use for it and provide another small step forward.

ODDS AND ENDS—A means for 'fixing' the position of sandbags on a bed has been described. The idea makes one jealous. Pillows are constructed with pockets for the sandbags, the leg is placed on the pillow between the bags, and the whole setup is thereby localized.

The Unitarian Committee of 5 clinicians and 5 basic science professors has just returned from an inspection of THE GERMAN PRACTICE OF MEDICINE. Dr. Dillon of Pasadena reports that medical service for most of the people is terrible, chiefly due to the war. Socialized medicine is of long duration, but in a sad status. The Hitlerian Reich had no notable effect on the system, since it was set before that time. (Most of the medical atrocities during the war were performed by mili-

tary rather than civilian physicians). . . . The educational situation contains many dreary aspects. Each basic science and clinical department has its own building. The former are beautifully equipped. The latter are self-sufficient units, with re-duplication of facilities and almost no consultation between services. The hierarchy of seniority is iron-clad, and the 'chief' is absolute boss over his underlings and patients. He is also very versatile in all branches of his specialty. . . . The status of students is most bleak. They study medicine for prestige; 3 out of 4 DO NOT INTEND to practice medicine; NONE will get a chance to practice unless he emigrates from Germany, since there are tens of thousands now waiting in line for licenses. Doctors can find no place to live, and they almost never move from the site of education.

The 'West Coast Druggist' has a column called 'Medical Progress' which is an odd combination of a pharmacy journal and the theatrical paper 'Variety'. . . . The terse style includes such abbreviations as '&', 'National Malaria Soc', 'phcy', 'Terramycin Cures', 'chlor-Trimeton Cited', etc. . . . An advertisement next to the column is even more intriguing. It says,—"Stick 'em up, Pardner (by the cash register that is); there's gold in them thar pills." The pills are "Sleep-eze", the 'non-habit forming sedative'. We may be intrigued into finding what they contain, and add it to this paragraph. . . . (The contents turn out to be hycosin, phenacetin, and sodium bromide).

Quote, from the Ohio State Medical Journal, "They are now saying that it is unwise to attempt treatment in cases of azoospermia and oligospermia without first performing a testicular biopsy, WHICH AFTER ALL IS A MINOR OPERATION." . . . The underlining is ours. There is probably none except our distaff colleagues who does not cringe at the thought of such a biopsy. It is the sort of loose talk which produces castration complexes, or maybe a phobia of urologists!

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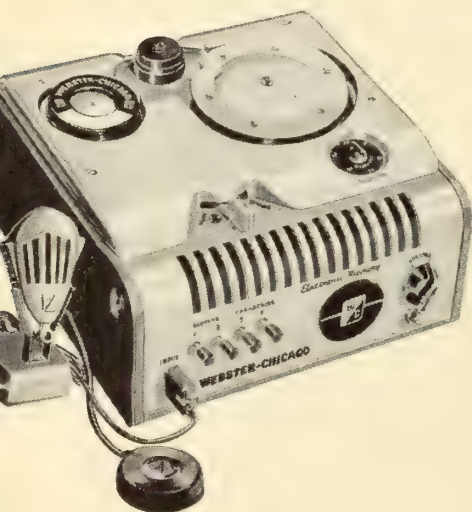
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PERSONAL NOTES

At the December 18th meeting of the Staff of St. Monica's Hospital Phoenix, the following officers for 1951 were elected. *Dr. Robert S. Flinn*, Chief of Staff; *Dr. Paul Jarrett*, Vice Chief of Staff; *Dr. A. I. Ramenofsky*, Secretary.

Dr. Joe Boyes, Los Angeles, California, spoke to the staff of St. Monica's Hospital, Phoenix on the subject of "Treatment of Hand Injuries."

Dr. D. A. Polson, Phoenix, addressed the staff of the St. Monica's Hospital, Phoenix, on a "Case Report-Arteriovenous Aneurysm About the Knee Joint." This was at the December 18th monthly staff meeting.

Dr. James M. Greer, Phoenix, leaves for Washington, D. C., January 11, 1951 to attend the session on procurement of medical officers for the armed services. He represents Arizona at the meeting. Bob Carpenter, Executive Secretary of the Arizona Medical Association will accompany Dr. Greer.

Dr. Clarence G. Salsbury, Phoenix, Chief of Preventive Medical Services of the State Department of Health, reported in the December issue of Arizona Public Health News, on the rather deplorable sanitary conditions in the migratory labor camps in Arizona. Physicians in these areas can help by promptly reporting communicable diseases in time to ward off serious epidemics.

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A direct writing electrocardiogram "Cardiotron" has been loaned to the Arizona Heart Association clinic at the Good Samaritan Hospital by the Waitt-Randolph Equipment Co., Phoenix.

This unit will be used as part of their cardiac survey.

The Waitt-Randolph Company also has available a motion picture of the research done by the E. R. Squibb Co. "Pronestyl Hydrochloride" and can be made available without charge at any clinic meetings.

undertake such a program and authorize the creation of a Grievance Committee.

The purpose of this Committee is to improve physician-patient relations and endeavor to moderate misunderstandings between the public and the profession. While the public relations value is purely a secondary consideration, the primary objective is to see that the public interest is fairly and honestly served and to correct misunderstandings and abuses which the patients think have occurred. Experience has proven where such course is pursued that it not alone builds for good public relations but in reality performs a service to the profession itself.

As in any trial procedure, certain "charges" were prescribed by the House of Delegates for Committee operation, and they are recited below for membership edification:

The Grievance Committee of this Association shall:

1. Act in fact as its "grand jury" for investigating complaints from both the lay public and within the profession concerning professional conduct and ethical deportment and likewise initiate investigations where, in the judgment of the Committee, it is determined advisable.
2. Initiate and prosecute, just as would a grand jury in civil proceedings, charges against any physician deemed by it guilty of unprofessional conduct.
3. Have no final jurisdiction in a judicial way. Just as would a grand jury, it shall receive and pass its own judgment upon evidence, but it shall not assume authority to discipline any physician. It shall lend itself to arbitration and may, at any time, express its advice and recommendation to Council or a member Society on any matter pertaining to professional conduct.
4. In pursuance of its function as a grand jury within the structure of the Association, the Committee shall have the power and authority to summon members of the Association to appear before it, either in connection with complaints involving the members summoned or as witnesses in cases involving other members. In the event any member should fail to respond to such summons, the Committee may determine to cite the member before the Council for contempt proceedings.
5. Be appointed by Council to include a total

YOUR GRIEVANCE COMMITTEE

In December, 1949, the House of Delegates of the American Medical Association, by resolution, voted commending those constituent State Associations that had already established committees to hear any complaints of the public and urged that all constituent Associations adopt comparable programs. Subsequently, through actions of your Council and House of Delegates in Annual Session this year, following exhaustive and deliberate study of the procedure with all its ramifications, it was determined to

of five selected from the panel of Past Presidents, none of which shall be active members of Council.

On January 7, 1951, your Grievance Committee met in Phoenix, Arizona, for the purpose of organization. George O. Bassett, M.D., of Prescott, was duly elected Chairman of the Committee, whose membership in addition to Dr. Bassett is presently composed of Dan L. Mahoney, M.D., Tucson; Hal W. Rice, M.D., Bisbee; and O. E. Utzinger, M.D., Ray. It is anticipated a fifth member will be appointed by Council shortly to complete the membership. Necessarily certain policy essential to the successful operation of this body was outlined, and the following rules and regulations of procedure adopted:

1. The main purpose of this Committee is to take preventive measures and a preventive attitude.

2. All complaints to be considered by this Committee received from either the lay public or within the profession must be reduced to writing and properly signed.

3. On all matters of unsatisfactory services and fees, a letter will be written to the physician with a copy of the complaint attached requesting his or her comment and report to the Committee, with the suggestion that the physician at that time endeavor to confer with the complainant on the charge in an endeavor to arrive at an amicable solution.

4. The complainant shall have acknowledgment of his letter and advised that the physician has been communicated with, a copy of the complaint filed with him and likewise suggesting that the patient take steps to confer with the physician in an endeavor to arrive at an amicable solution.

5. The physician charged with a complaint will be requested to submit his report within 10 days from receipt of notification of the filing of the charge and a follow-up letter forwarded upon failure so to do.

6. On filing of the physician's report the Committee shall decide whether the grievance is justified and what action shall be taken.

7. If the complaint cannot be satisfactorily adjudicated between the two individuals and the complaint in the opinion of the

Committee seems justified and it seems advisable, the Committee will continue further investigation and will request that the two interested parties appear before the Committee to be heard individually at a specified time and place.

8. In all instances where the Grievance Committee cannot successfully adjudicate the differences between the complainant and the physician, wherein the physician refuses to abide by the recommendation of the Committee, a copy of the file shall be forwarded to the respective county medical society for any action it shall deem necessary.

It was the unanimous viewpoint of the Committee that it should be called together in meeting at sufficiently frequent intervals in order that no case will go without decision for an unreasonable length of time.

It was further determined in the instance of Maricopa County and Pima County Medical Societies wherein a similar Grievance Committee has been organized and is operating, that they be notified of the receipt of any and all complaints filed with this Committee involving a member of its society, furnishing said Committee with a copy of the complaint so received and requesting that said Committee immediately advise the state Grievance Committee whether or not it may elect to consider the charge or whether it is the desire that the state Committee shall handle the case. In the instance where a society Grievance Committee elects to handle the complaint it shall be requested that a copy of its findings and decision be filed with the state Grievance Committee.

The Arizona Medical Association is proud to be listed among those 34 of the American Medical Association's 48 constituent State Medical Associations who have thus demonstrated their continued interest for the welfare of their physicians' patients, and calls for the full support and cooperation of all those concerned. As commented upon recently editorially: "Thrashing out differences usually promotes better understanding. The members of the Arizona Medical Association have recognized that these truths apply to their business—and their customers—just as they do in other fields . . . seeking a sympathetic understanding with their 'customers,' the profession is effectively combatting trial of England's health plan here."

BOOK REVIEWS

Methods in Medicine, The Manual of the Medical Service of George Dock, M.D., Sc.D. formerly Professor of Medicine, Washington University School of Medicine; Formerly Physician-in-Chief, Robert A. Barnes Hospital, St. Louis by George R. Herrmann, M.D., Ph.D., Professor of Medicine, University of Texas Medical Branch at Galveston; Director of the Cardiovascular Service and Heart Station, University of Texas Hospitals. Consultant in Medicine to the Surgeon General, U. S. Army; Consultant in Vascular Diseases to the Marine Hospital, U.S.P.H.S. Second Edition, Completely revised. A volume of 488 pages, published by The C. V. Mosby Company, St. Louis, 1950, Price \$7.50.

This reviewer is amazed at the amount of practical information contained in one comparatively small volume. Furthermore this information is orderly arranged so that information needed on any one subject is either found altogether in the same place or made easily available elsewhere by easy cross reference methods. The information for the most part is specific, brief, unencumbered by necessary detail and is surprisingly up to date. It is a pleasant surprise to note how many of the very recently discovered drugs are mentioned and directions for their use given in conditions in which they are indicated.

The book is divided into five parts entitled (1) Methods of Routine Case Study, (2) Clinical Laboratory Procedures and Tests, (3) Methods of Clinical Investigation, (4) Therapeutic Methods, (5) Dietetic Methods. In the first part there is a chapter on history taking and

physical examination giving a detailed outline with sufficient explanatory notes for taking the general history, review of systems, routine physical examination and a brief guide for other studies in doing a complete study on a patient. In other sections of the book most of the usual and many of the unusual laboratory examinations are given with the technics for many of them being given in the book and references as to where technics can be found given for some of the more unusual procedures. There is an outline for the management of the various emergencies, outlines for studies of various types of disease conditions and directions for various therapeutic procedures even including directions for Scotch douche. In the section on dietetic methods, many useful and specific diets are given, as for example the many types of ulcer diets which have appeared in medical literature and been found useful. These are brought together and made available in one place.

I think any medical student would prize this book very highly and use it very much. The practicing physician, I feel, would find it very useful as a desk reference.

R.L.F.

The following footnotes were omitted in the January, 1951 issue on Dr. Winona G. Campbell, "Read before the Arizona Medical Association Annual Meeting, Tucson, Ariz., May, 1949," and Drs. Chas. A. Janda and Arie C. Van Ravenswaay, "Read before the Arizona Medical Convention, Annual Meeting, Phoenix, Arizona, May, 1950."

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CANCER SYMPOSIUM

On March 1 and 2, 1951, the "Fourth Utah Cancer Symposium" will be presented by the University of Utah Medical School, in conjunction with the Utah Chapter of the American Cancer Society, the Utah State Department of Health, and the Utah State Medical Association. The scientific sessions will be held in the Amphitheater of the new Nurses Home of the Holy Cross Hospital, Salt Lake City, Utah.

The aim of the program is to present information of value to the practicing physicians. This information will be presented in the form of clinics, seminars, talks, conferences, teaching movies, and round table discussions. Dr. Louis A. Buie, from Rochester, Minnesota, will discuss diagnosis and therapy of rectal lesions. Dr. Charles Huggins, from Chicago, will present the problem of prostatic cancer as it presents itself to the general practitioner; he also will conduct a seminar on cancer tests. Dr. Ralph Bowers, from Memphis, will discuss gastric cancer, and an "unknown case" at a clinical pathological conference, together with Dr. Lauren V. Ackerman, author of the well known textbook on Cancer. Dr. L. Henry Garland, from San Francisco, will present the radiologist's aspect of gastric cancer, and conduct a seminar on unusual x-ray films. Dr. Allen Barnes, from Columbus, Ohio, will discuss the position of the general practitioner in the fight against early cervical cancer, and conduct a conference on recent advances in late cancer therapy. Of special interest will be two round table discussions, one on early cancer diagnosis, and another on late cancer therapy. The moderators in these discussions will be Dean John Z. Bowers, and Dr. Maxwell M. Wintrobe; the discussers will be the guest speakers.

Special preparations are being made to entertain the physicians' wives, who are cordially invited to attend. It is planned to have a fashion show, a cocktail party, banquet and other entertainment. The meeting is expected to be a memorable event both for the physicians and for their wives.

WESTERN CONFERENCE ANNOUNCES THEME

"Circulation" will be the theme for the Second Biennial Western Regional Conference on Anesthesia to be held at the Hotel Del Coronado, San Diego, on April 2-4, 1951. Many leading anesthesiologists and specialists in related fields

have already been scheduled for program participation. The program will be presented immediately preceeding and at the same place as the oral examination of the American Board of Anesthesiology. Extensive entertainment events, including attendance at the Jai Alai games in Tijuana, a cruise in the Bay, tours and other entertainment for the ladies, and a Dinner at which Admiral Stanley, former Ambassador to Russia, will speak, have been planned. It is not too early to make your reservations.

Don't miss it! Besides such well known names in anesthesiology as Doctors Macintosh, Dripps, Cullen, Leigh, Dillon, McQuiston, Pender, Scott Smith and Fisher the program is also studded with outstanding scientists in related fields including Victor Hall, M.D., Professor of Medicine, University of Southern California Medical School, Charles P. Baker, M. D., Director of Pathology, Samuel Merritt Hospital, Oakland, Calif., John C. Jones, Los Angeles, Maurice H. Seevers, M.D., Professor of Pharmacology, University of Michigan, Marcus A. Krupp, M. D., Assistant Clinical Professor of Medicine, Stanford University Medical School, William Paul Thompson, M.D., Clinical Professor of Medicine, College of Medical Evangelists and William P. Longmire, Jr., M.D., Professor of Surgery, University of California Medical School at Los Angeles. These outstanding participants on the Scientific Program together with the galaxy of social events planned for those who attend, makes this meeting a number one must on your schedule.

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WOMAN'S AUXILIARY YAVAPAI NEWS

Mrs. James H. Allen, an outstanding member of the Yavapai Auxiliary for many years as well as being a former state Auxiliary president has been guiding the Yavapai group's activities as the 1950-51 president. Being one of the auxiliary's organizers, Mrs. Allen has served as president several times and has worked in countless other capacities over the years.

The group's most recent project was a benefit dessert bridge and canasta party. The proceeds were used to finance the Yavapai contribution to the Student Nurses' Loan Fund. Other immediate plans include aid in the form of clothing, food, and toys to needy families at Christmas.

Mrs. M. W. Phillips (Prescott)

MARICOPA COUNTY

Mrs. Archie E. Cruthirds, first vice president, presided at the December meeting of the Maricopa County Medical Auxiliary, in the absence of the president, Mrs. Karl S. Harris. The meeting was held in the Good Samaritan Nurses' Lounge.

In preparation for the Christmas party which the Auxiliary is planning for the children at the County Hospital, each member brought a gift for a child, and books for a permanent library. Mrs. J. H. Patterson is going to make a candy cane for each child.

At the conclusion of the business meeting, the nurses presented a Christmas program, introduced by Mrs. Goldenburg, Director of Nurses at Good Samaritan Hospital. Under the direction of Mr. Hollis Dindot, music teacher in the city schools, the nurses sang a group of Christmas carols. Miss Mary Jane Felgar read the lovely Christmas story, "Why the Chimes Rang," and Miss Louise Huber sang a solo. Miss Paula Duffy, costumed as "Mrs. Santa Claus" presented a dance, after which she distributed candy canes from her pack.

After the entertainment, Mrs. J. W. Findley Jr., Hospitality Chairman, introduced five new members with a brief biographical sketch of each. Mrs. F. B. Laneback, and Mrs. J. Edwin Keppel of Mesa; Mrs. C. Thomas Read, Mrs. J. Martinek, and Mrs. James Coffey of Phoenix.

The social hour followed and refreshments were served by a committee headed by Mrs. Frederick D. Baier.

Respectfully submitted,
Mrs. John Eisenbeiss Phoenix

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MEDICAL GROUP HOLDS OPEN HOUSE, SUPPER

Reprinted from Tucson Star

Pima County Medical Society and auxiliary held an open house and buffet supper at the Wild Horse ranch from 5 to 8 p.m.

Hosts and hostesses were Drs. and Mmes. Kirby W. West, Ian M. Chesser, M. A. Carreras, Hollis H. Brainard, Maxwell Palmer, Donald B. Lewis, Darwin Neubauer, S. I. Shapiro, Willard L. Strode, Kenneth Baker.

Drs. and Mmes. Ralph H. Fuller, Hugh Thompson, John Stacey, Arie C. Van Ravenswaay, Harold E. Kosanke, Alex Shoun, Leo Kent.

Reservations were made by 328 local doctors and their wives.

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MRS. ROY HEWITT

President of Pima County Medical Auxiliary

Mrs. Roy Hewitt is President of the Pima County Medical Auxiliary. She was born in Seattle, Washington, but lived in Kansas and Missouri before moving to Arizona in 1924. Mrs. Hewitt attended Kansas State College at Manhattan, Kansas and graduated from the University of Arizona. A year's post graduate work in dietetics was received at the Michael Reese Hospital in Chicago. Before her marriage to Dr. Hewitt in 1934 she worked as a dietitian at St. Mary's Hospital, Tucson, and the Veterans Hospital, Bronx, New York.

She served as 2nd vice-president of the Pima County Auxiliary in 1946 and 1947 was State Bulletin Chairman of the Arizona State Medical Auxiliary.

Mrs. Hewitt was chairman this fall of the annual Silver Tea given by St. Lukes on the Desert, Board of Visitors.

She's Past Placement Chairman and past chairman of Children's Theatre and past chairman of Rolling Library at Pima County Hospital for the Junior League of Tucson.



Left to right: Mrs. L. L. Stolfa, Mrs. Wm. H. Cleveland, Mrs. Clark L. McVay and Mrs. Paul S. Causey, all of Phoenix, Arizona.

VISITING NURSE SERVICE

At the first annual meeting of the Woman's Auxiliary to the Maricopa County Medical Associations, it was decided to do volunteer work for the Visiting Nurse Service.

The Visiting Nurse Service of Phoenix was established in January, 1946. The purpose of the service is to provide part-time bedside nursing care in the home of anyone living in Metropolitan Phoenix, who is under the care of a recognized local physician.

In May, 1949, the Visiting Nurse Service Auxiliary was organized. This is a "booster" group, giving time, money, and energy to the work of the agency. Members of the Auxiliary lend helping hands to routine tasks, guaranteeing the nurses a maximum of time for actual bedtime care. The members prepare supplies, sew, wrap dressings, cut cotton, and contribute typing and filing hours to the clerical division. In addition, they collect magazines and books for the service's lending library and provide a motor corps for driving student nurses to their patient's homes. This year the V.N.S. Auxiliary is preparing bedside trays and potted plants to be distributed to the patients at Christmas.

Members of the Medical Auxiliary have volunteered to assist with these tasks. Two women are giving a half day each week. Mrs. Donald Carlson, who is Health Chairman of the Medical Auxiliary, is in charge of this project.

Respectfully submitted,

Mrs. John Eisenbeiss—chairman
Mrs. L. L. Stolfa—co-chairman
Phoenix



Mrs. John W. Findley, Jr., Phoenix

HOSPITALITY

This year the Maricopa County Medical Society is promoting a "Get Acquainted" program between the wives of doctors recently taken into the County Medical Society and the wives of established doctors. At each meeting several newcomers are introduced. The audience is told where the doctor was born and educated and his field of medicine. We also learn the wife's native state, her places of education and the size of her family. These facts establish a bond among Auxiliary members and offer good conversation material. Thus far seven newcomers have been introduced. They are Mesdames Fred Ewart, John Ford, Robert Ripley, John McKenna, James Barger, Fred Coleman, and John Kennedy.

Mrs. John W. Findley Jr. originated this plan which is working very successfully. Both Dr. and Mrs. Findley were born and raised in Indiana. They were graduated from Purdue University in 1940. Mrs. Findley then worked on the campus at Purdue and later for the C.A.A. as an Airport Traffic Control Tower Operator. She and Dr. Findley were married in 1943.

Doctor Findley received his M.D. at the University of Chicago, interned at Yale, served with the Navy, and spent three years in residency in the Department of Medicine in the University of Chicago's Billings Hospital. The Findleys came to Phoenix in September, 1949. They have two handsome boys, Tom, 5, and Bill, 3.



Left to right: Mrs. Roy Hewitt, President, Mrs. Leo J. Kent, Vice-President, Mrs. Hugh Thompson Legislature Chairman, and Mrs. Richard Hausmann, Program Chairman, all of Tucson. The above women were attending the first general meeting and plans were discussed for the Nurses Loan Fund project for the Community Chest.

Mrs. Findley is active in the Phoenix Symphony Guild, Fine Arts Association, and the Medical Auxiliary. Her work for the Auxiliary has been enthusiastically received; it may be hoped that the program will continue for many years in order that the Maricopa County Auxiliary may become a more closely knit, useful organization.

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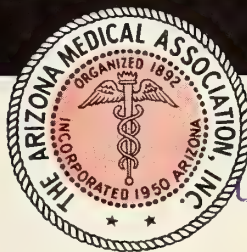
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(1) Raydin, I. S., and Gimbel, N. S.: Protein Metabolism in Surgical Patients, J.A.M.A., 144:979 (Nov. 18) 1950.

(2) Vars, H. M., and Gurd, F. N.: Role of Dietary Protein in Experimental Liver Regeneration in Nitrogen Balance Study, Am. J. Physiol., 151:391 (Dec.) 1947.

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ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 3



MARCH, 1951

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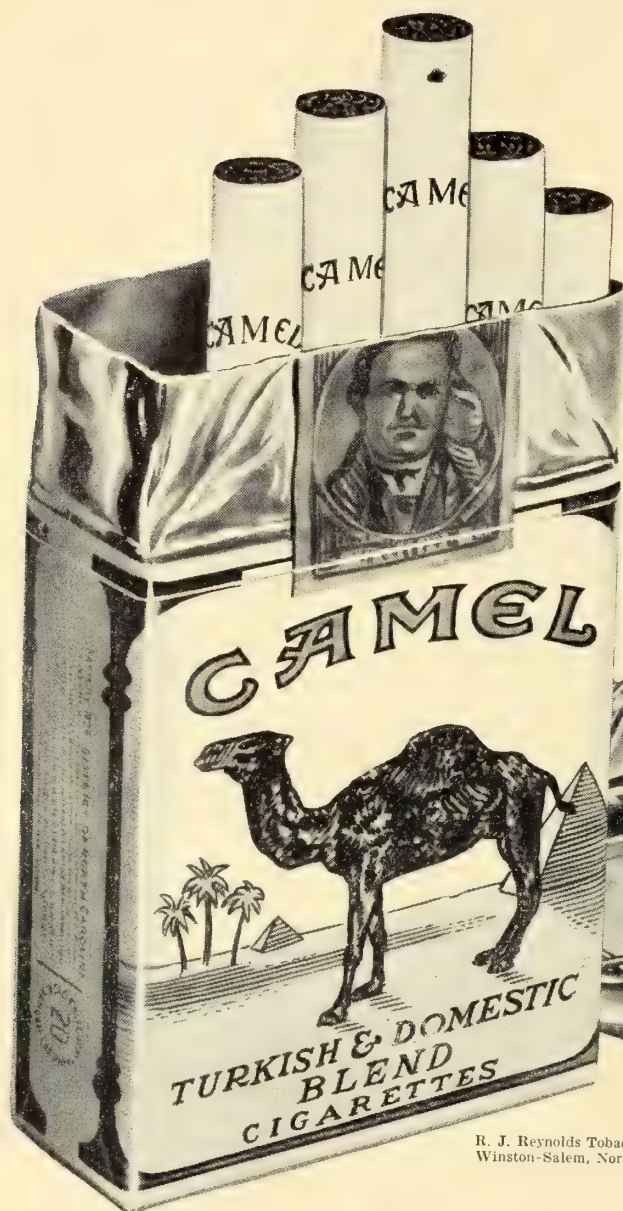
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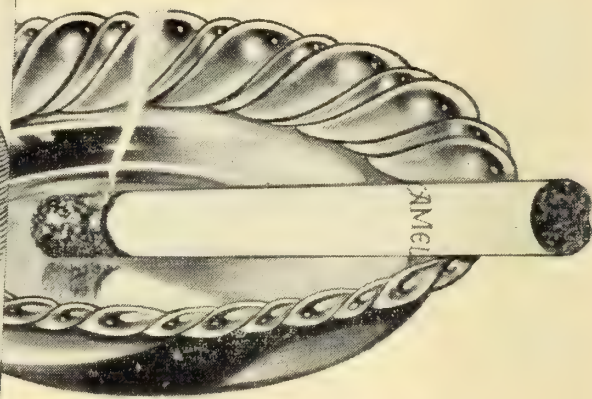
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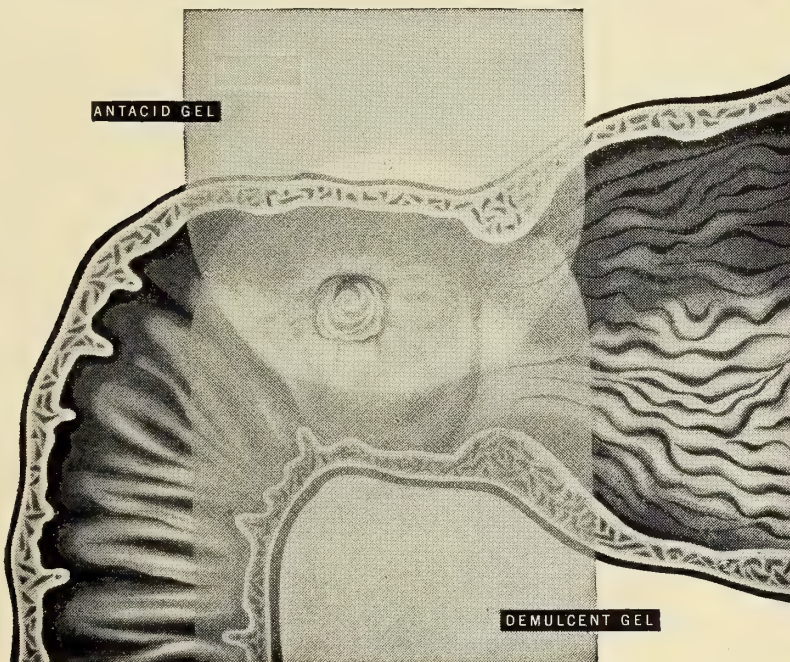
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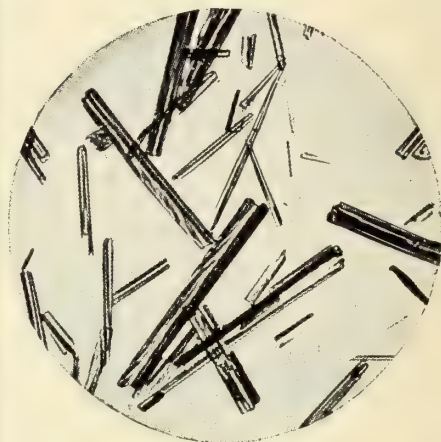
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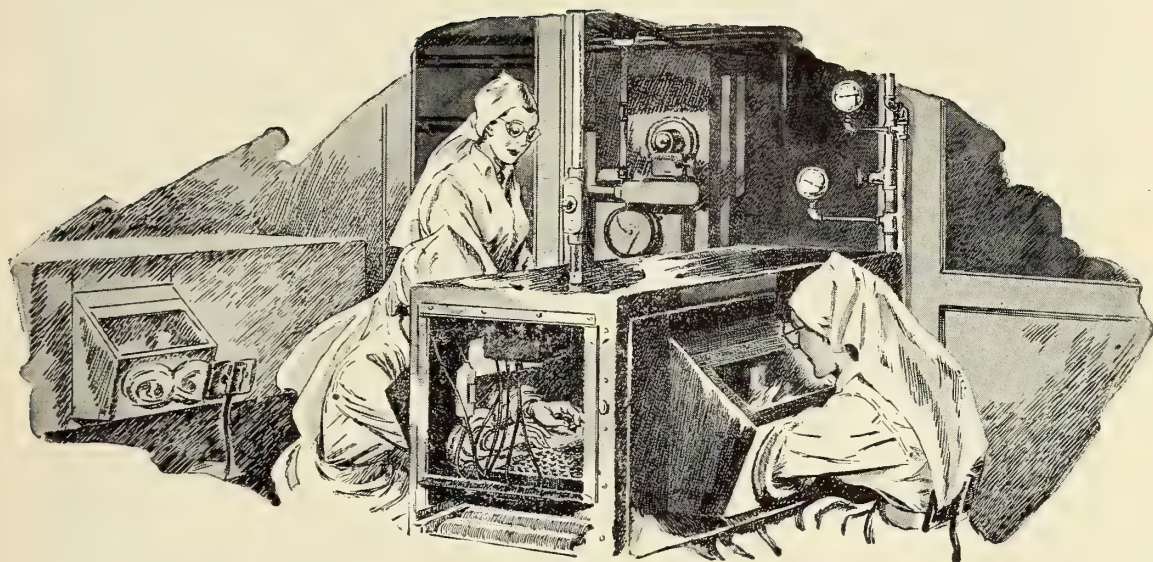
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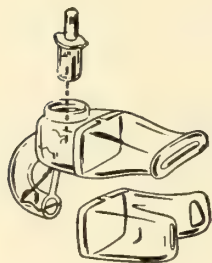


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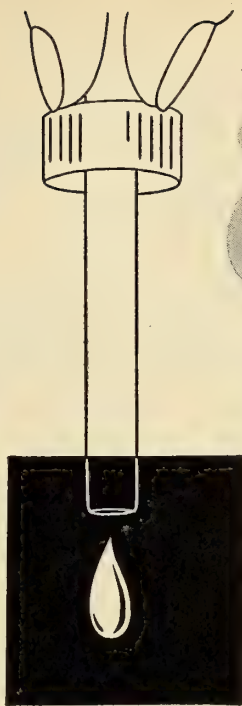
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		SOURCE	ORGANISM			
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Dowling, H. T.; Lepper, M. H.; Caldwell, E. R., and Spies, H.: Ann. New York Acad. Sc. 53:433 (Sept.) 1950.

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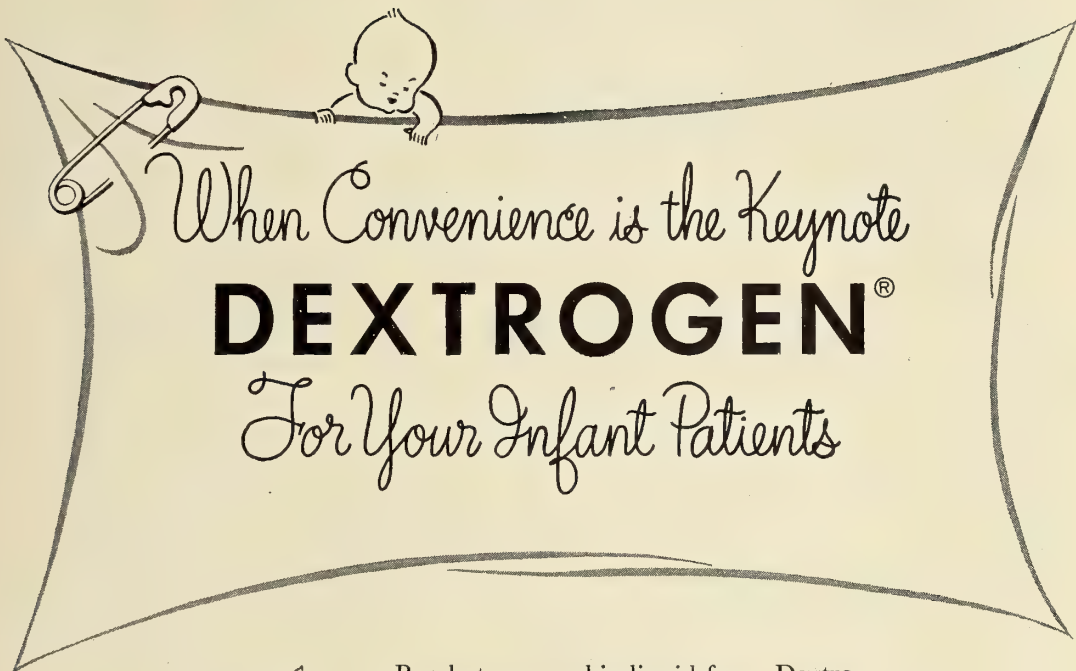
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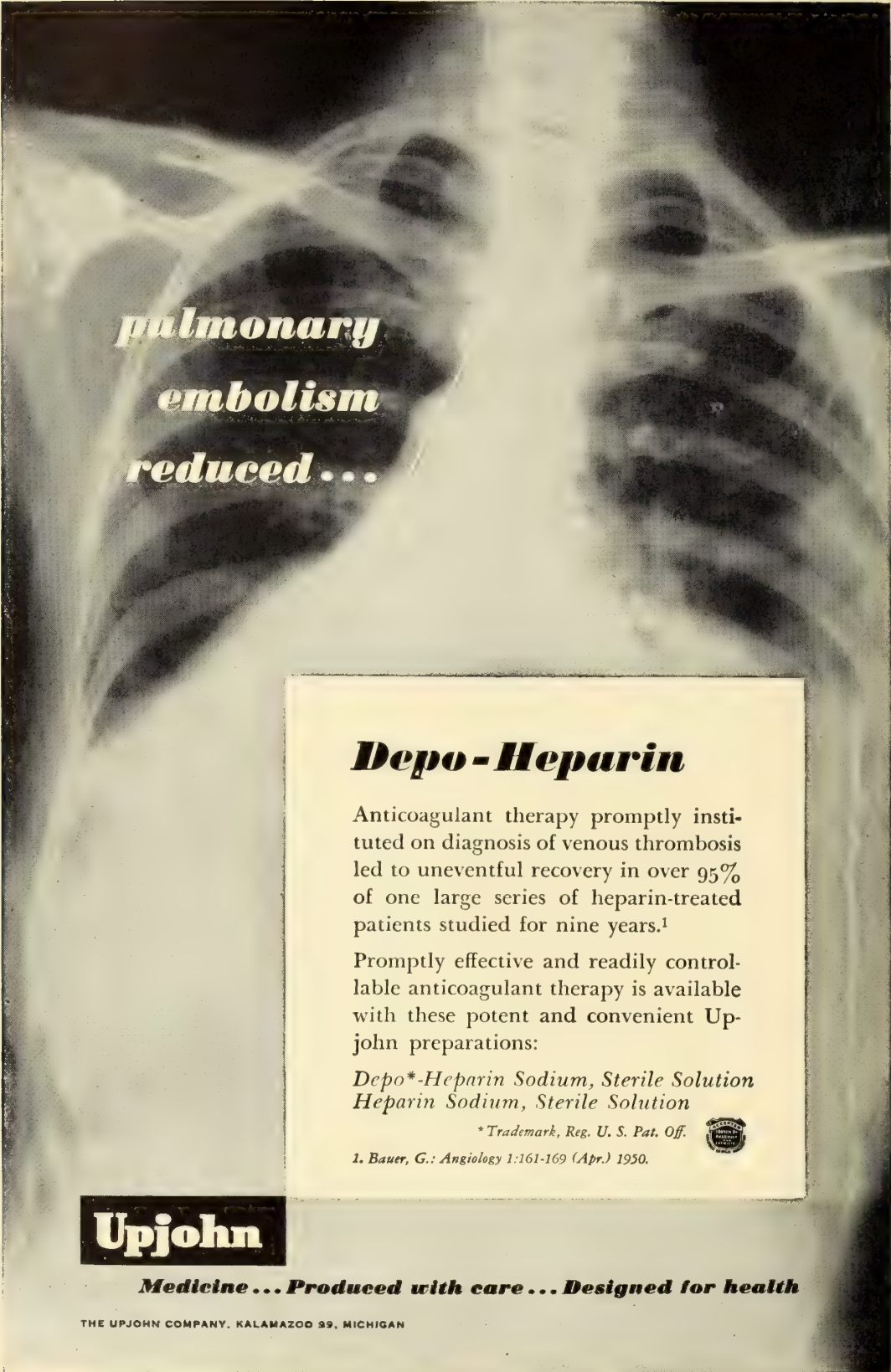
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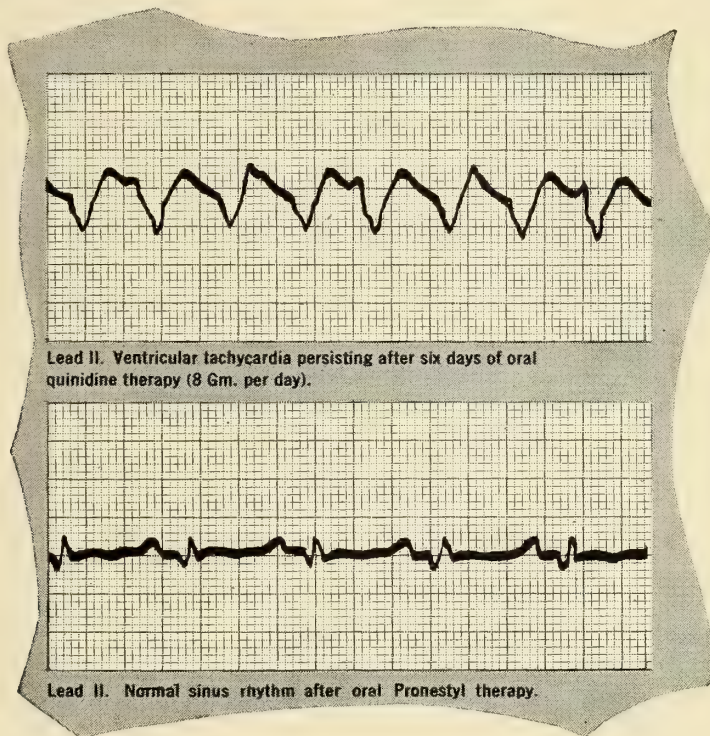
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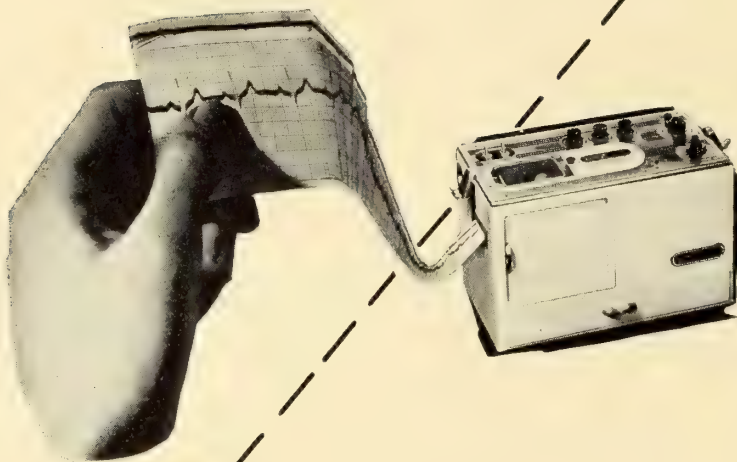
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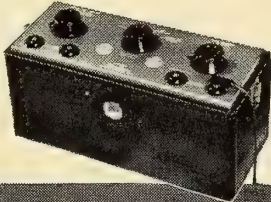
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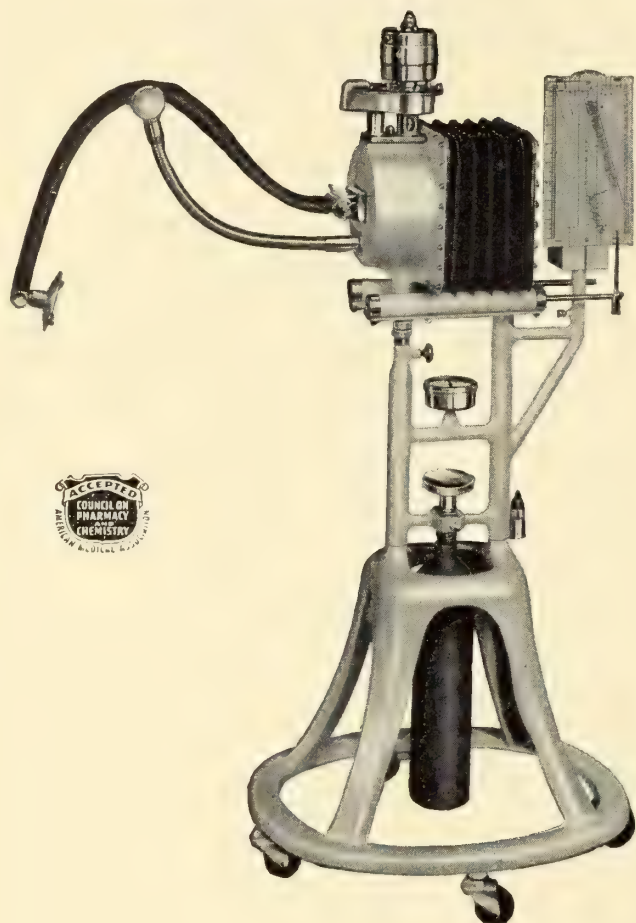
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Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 3



MARCH, 1951

INDICATIONS FOR RESECTION IN PULMONARY TUBERCULOSIS*

PAUL C. SAMSON, M. D.**

Oakland, California

Resection as a treatment in pulmonary tuberculosis is now undergoing a third wave of restrained enthusiasm. The first period in the modern era was approximately from 1935 to 1940 and coincided with the development of individual ligation technique in pneumonectomy and preliminary improvements in anesthesia. Early optimism was followed by extreme pessimism particularly in relation to lobectomies; inevitable empyemas and bronchial fistulae accompanied tourniquet ligation in lobectomy and these were frequently followed by both early and late tuberculous spreads. Such complications proved to be much more serious in patients with tuberculosis than in patients with chronic non-specific suppuration. The second (or pre-streptomycin) period occurred between 1940 and 1946, and followed the standardization of individual ligation technique for lobectomy, further improvements in anesthesia and the free use of blood replacement therapy. Early empyemas and fistulae were greatly reduced but there were late infections and reactivations which left five-year end-results with much to be desired (1). Another factor, at least in certain series, was the mistaken idea that the tuberculous infection could be totally removed by lobectomy or pneumonectomy. Many patients were not kept at bed rest for a sufficient period of time following resection. Thus, a group of 30 patients who were not subjected to bed rest following resection has been investigated by Dugan (2). Immediately following operation there was one death (3.3%) and three spreads (13%). Nine months later there had been two additional deaths from tuberculosis (10%) and seven additional spreads of tuberculosis (36.6%).

The present or third period is the era of antibacterial therapy and commenced when streptomycin (more recently PAS and Tibione) became available in 1946. Comparative studies (3) (4) (5) now indicate unequivocally that surgical prophylaxis with streptomycin has greatly reduced the immediate hazards of resection in tuberculosis. The specters of fistula-empyema, spreads and reactivations are much less frightening than before. We have come to realize, too, that seldom, if ever, is all the tuberculosis removed. A period of bed rest, preferably for six months, should certainly follow resection. The elapsed time is too brief to tabulate later results, but the indications are that they will be appreciably better than in the pre-antimicrobial era.

It is important to state here our conclusions concerning the administration of streptomycin and PAS. Early enthusiasms and lack of precedent led to larger dosage regimens than are now considered necessary. Types of disease now known to respond poorly were originally treated uncritically. The history of these trials and tribulations is common knowledge and I will not elaborate. Suffice it to say the emergence of resistant strains has been of great concern to the surgeon as well as to the internist. In our experience, patients whose bacilli were highly resistant to streptomycin have been poor candidates for resection. Jones and Robinson (3) believe such a situation may actually be a contra-indication to resection. They operated on eight patients who were streptomycin-resistant and all developed serious complications. Whether or not PAS alone, perhaps reinforced with intravenous PAS during the immediate post-operative period, will be an adequate substitute in patients with streptomycin-resistant organisms is a subject for present and future investigation.

*Presented at the Annual Meeting of the Pima County Medical Society at the Veterans Administration Hospital, Tucson, Arizona, May 9, 1950.

**Associate Clinical Professor of Surgery, Stanford University School of Medicine; Area Consultant in Thoracic Surgery, Veterans Administration.

The obvious corollary is that streptomycin cannot be given indiscriminately with impunity. Certain care and judgment must be exercised in its administration under a medical regimen. It should be standard procedure that where streptomycin boards exist, a thoracic surgeon should be a member of the team. The possibility of eventual resection may then be more adequately assayed and the early administration of streptomycin for the patient in question more intelligently regulated. Since the combined administration of streptomycin and PAS delays the emergence of resistance these drugs always should be given together. With the information now available, a safe intermittent dosage-schedule may be selected for the initial regimen. A later intensive course may be so timed that resection can be performed within the period of expected sustained sensitivity.

CONTRAINDICATIONS TO RESECTION

Certain contraindications to pulmonary resection should be briefly discussed. (1) In general, patients with other difficulties such as cardiovascular renal disease, etc., are not good subjects for resection. The patient must be fit for major surgery. A moderate decrease in pulmonary function may not be a contraindication to resection. Thus, Gaensler and Strieder (15) have shown that there is no great difference between lobectomy and thoracoplasty in decreasing pulmonary function. (2) Ulcerative tuberculous bronchitis. To me, this is an absolute contraindication to resection. Incision through a bronchus which is actively diseased is an open invitation to fistula and empyema. (3) Acute exudative disease on either side contraindicates resection at the time. Active disease in the contralateral lung, *per se*, if it is controlled and stable does not contraindicate resection if the pulmonary function is adequate. In this situation, antimicrobial therapy may be administered for a longer period of time after operation than would ordinarily be employed for surgical prophylaxis. Pneumoperitoneum and pneumothorax likewise should be considered as important factors of the post-surgical therapeutic program.

GENERAL INDICATIONS

There are two general situations in which resection may be indicated. The first of these concerns the status of the bronchial system. I agree with Jones that various aspects of bronchial disease are fruitful sources of resection material.

Bronchial stenoses may affect the stem bronchus. This ordinarily leads to consideration of pneumonectomy since lobectomy is not a safe procedure distal to a stenosis. In cases of lobar stenosis, lobectomy should be considered. It is of importance that the upper lobes be directly inspected with a right angle telescope if stenosis of these bronchi is to be accurately diagnosed. Intrapulmonary tuberculous bronchitis and bronchiectasis if diagnosed or suspected would make resection the more logical procedure.

The second of the situations regards the type and position of cavities, and their reaction under pneumothorax, pneumoperitoneum or incomplete thoracoplasty. Giant or tension cavities are known to be notoriously difficult to close with thoracoplasty. While it has been done successfully, it is usually at the expense of an increased number of stages and a probable undue decrease in pulmonary function. Cavities in the anterior segments of the upper lobes, the right middle lobe, the lingula or in the lower lobes are likewise difficult to collapse by thoracoplasty. Resection should be considered for cavities in these locations and is by all odds the treatment of choice in middle and lower lobe cavities. Certain cavities balloon or show sudden decreases and increases in size under pneumothorax and pneumoperitoneum. Some of these cavities show no decrease in size even with extensive pneumothorax. Cavities of this type are not favorable for thoracoplasty and resection should be considered. The behavior of a cavity following one or two stages of a thoracoplasty may counsel resection. If the cavity increases in size, particularly if it balloons up *above* the unresected ribs, the next operation usually should be resection rather than further stages of a thoracoplasty.

If resection is decided upon, no commitment should be given the patient for segmental resection, lobectomy or pneumonectomy. In general, resection should be aimed at saving relatively normal parenchyma. It is often a matter of fine judgment at the time of operation to decide upon the limits of resection. The choice of procedure is determined by the amount and type of disease seen in the x-ray and palpated in the lung, and the location of stenoses. In rare instances, a contemplated lobectomy becomes a pneumonectomy because of technical difficulty with adhesions, the complete loss of normal fissural markings and operative accidents (tearing of arteries).

There are certain commonly accepted specific indications for resection in tuberculosis.

1. *Unsuccessful Thoracoplasty.* Sharp distinction should be made between lack of success because of a technically poor thoracoplasty and an adequate thoracoplasty which fails because of the type of disease. If the patient has been improved and the disease brought under partial control by a poor thoracoplasty, a revision operation probably should be performed in preference to resection. Certain types of disease, however, mitigate against success in thoracoplasty: bronchial involvement, thick-walled cavities and giant or tension cavities. If such exist, resection is to be preferred rather than secondary (revision) thoracoplasty.

2. *Destroyed Lung.* A lung may be destroyed because of extensive tuberculous disease throughout or because of the presence of secondary suppuration or bronchiectasis. Thoracoplasty has little to offer in either situation. I believe it to be actually contraindicated if clinical pyogenic infection is present.

3. *Tuberculoma.* This broad term is probably employed too loosely in many instances. It covers, however, true granulomas of the lung as well as the solid rounded shadows which eventually prove to be thick-walled cavities filled with partially inspissated caseous debris. It is common experience that collapse procedures have little to offer in the permanent control of these lesions. Since it has been proved that there is an appreciable risk of spread if the lesions are untreated, resection appears to be the treatment of choice. There has been considerable discussion as to whether such lesions should attain a critical size before removal becomes advisable; there is no absolute answer to this question at present. It is probable that any lesion which increases in size should be removed but I hesitate to remove a tuberculoma which is less than a centimeter in diameter unless the exact nature of the round shadow cannot be determined by appropriate tests.

4. *Problems of the Unexpanded Lung.* In certain patients with unexpanded lung, resection should be considered as one facet of a combined surgical attack. The dictum of preservation of relatively normal parenchyma makes some of these problems quite difficult from the surgical point of view, since it is far easier technically to perform a pneumonectomy. Evaluation of the pulmonary condition prior to pneumothorax is

of the utmost importance since the success of decortication is dependent upon at least one expandable lobe. In this situation, it makes no particular difference whether the non-expansion is complicated by pleural effusion or by a tuberculous empyema. If one of the lobes contains persistent active disease or a cavity, decortication should be combined with lobectomy. Thoracoplasty should be done at the same time or as soon as possible to prevent over-expansion of the remaining lobes. If there is inactive disease in one lobe but the lobe is fibrotic, decortication should be performed on the relatively normal lobe and a small thoracoplasty done at the same time to collapse permanently the non-expandable lobe.

NEWER TECHNIQUES COMBINED WITH RESECTION

Within the past two years, several techniques have been developed which have as their aim both the extension of indications for lobectomy and the increased preservation of relatively normal parenchyma. It is important to discuss these techniques briefly in the light of their probable worth.

Chamberlain (6) (7) has interested himself in segmental resection for tuberculous lesions. While segmental resection, in general, has been practiced with increasing frequency during the past few years, Chamberlain is the first so far as I know to apply the technique intensively to excisional problems in tuberculosis. Recently, he reported his experiences with one hundred segmental resections. There was a 3% mortality. Chamberlain stresses that he removes only the main offending lesion and deliberately leaves behind modular disease on many occasions. He has found that lateral tomography is of great assistance in deciding upon the extent of segmental resection. Late results cannot be reported at this time but segmental resection undoubtedly has considerable merit in many cases.

Sarot (8) has recently published his experiences with extra-pleural pneumonectomy and pleurectomy. He and his coworkers are convinced that the pleura itself is a tissue showing marked decreased resistance to tuberculous infection and believe it should be removed almost routinely in pneumonectomy. The use of this technique likewise has made possible the removal in toto of a badly diseased lung and extensive empyema without actually entering the pleural cavity and, therefore, without contamina-

tion of the intrathoracic space or the operative field.

Gebauer (9) (10) has investigated the possibilities of plastic reconstruction of stenosed bronchi by means of dermal grafts. Rarely pneumonectomy has been necessary because of high grade stenosis of the main stem bronchus, when the active disease was confined to an upper lobe. This has resulted in sacrifice of completely normal parenchyma on more than one occasion, since lobectomy distal to a stenosis is not a feasible procedure. In a number of instances Gebauer has been able to save a normal lower lobe by proceeding with the indicated resection, then incising through the stenosed bronchus posteriorly and enlarging it by means of a dermal graft. The procedure is a highly technical one but has enjoyed considerable success in Gebauer's skillful hands.

There is general agreement among thoracic surgeons that over-expansion of remaining lung tissue following lobectomy in tuberculosis is undesirable. In most instances, a delayed thoracoplasty has been performed to prevent over-distension but we believe that even short term over-expansion should be prevented if possible. Following Iverson and Skinner's (11) reports of pneumonectomy and concomitant thoracoplasty which appeared 14 months ago we became interested in this problem and proceeded with primary upper lobe lobectomy and concomitant thoracoplasty in a number of patients (12). Experience during the past 14 months with some 25 cases has proved that there is no additional morbidity or mortality if a limited thoracoplasty is combined with lobectomy. Our preliminary results has been sufficiently gratifying so that the combined procedure is now used almost routinely with primary upper lobectomies.

THORACOPLASTY VERSUS PRIMARY RESECTION

In any clinic where an appreciable number of resections are performed, there are well known difficulties in attempting uniformly to decide what constitutes an indication for primary lobectomy. The success or failure of the surgeon with both lobectomy and thoracoplasty (including his most recent case) varying attitudes of the medical consultant, the individual interpretation of roentgen films in regard to the actual pulmonary pathology, the general status of the patient, and the bronchoscopic findings are all factors which need but to be listed. There is likewise

the growing realization that thoracoplasty may not be the ideal operation for all chronic tuberculosis; that thoracoplasty results differ considerably if the type of pulmonary pathology is taken into consideration. The recent report of Rubin and Klopstock (13) and Steele's editorial (14) stress the validity of this concept in an excellent manner. With these factors in mind, the history, pre-operative estimation of pathology and post-operative specimens were reviewed in a series of 35 primary upper lobectomies. Over 50% demonstrated pre-operatively what were believed to be primary indications for resection, following the suggestions of Rubin: giant or tension cavities, solid lesions, secondary pyogenic infection, lobar stenosis, and extensive bronchiectasis. Prior to operation the remainder were thought to be purely elective resections (that is lobectomy was elected instead of thoracoplasty) but in approximately three-fourths of these the surgical specimens showed combinations of thick-walled cavities, bronchiectasis, extensive intrapulmonary ulcerative tuberculous bronchitis, fibrosis, and lobar distortion. Rubin stresses that these conditions definitely militate against a successful thoracoplasty.

There still remains a group of patients in whom thoracoplasty is highly successful. In most instances, this group forms by far the largest percentage of any thoracoplasty series. These are the patients with fibro-caseous tuberculosis, characterized by predominantly productive stable lesions associated with small or medium sized cavities. In cases of this sort, thoracoplasty will afford a high percentage of cures.

It must likewise be emphasized that the overall mortality in resection is appreciably greater than it is in thoracoplasty. In selected groups, however, particularly in those where resection is an elective procedure, the differences in mortality rates are greatly diminished.

CONCLUSIONS

I have indicated to you some of my thoughts regarding the present indications for resection. It is a more complicated business than it was fifteen years ago when, if major surgery was considered, thoracoplasty was almost the universal choice. I emphasize that even now in many clinics thoracoplasty would be preferred to resection for many of the patients on whom I and others have performed lobectomy and pneumonectomy. I emphasize, too, that thoracoplasty probably would be successful in a fairly large

percent but at the expense of many more operations and, perhaps, an increased sacrifice of pulmonary function.

Further study of the essential pathology for which we operate is the crux of the matter. In the future I venture to predict that the percentage of patients for resection will increase while the percentage of patients for thoracoplasty will show a gradual decline.

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CHLOROMA (A CASE REPORT)

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We believe that it is of general interest to present this clinical case whose study has been possible to perform in due form, because of its rarity and also its typical manifestations. For this reason we reduce this paper to its simplest form restricting it to the purpose of this meeting.

This case is of particular importance from the standpoint of the differential diagnoses of exophthalmos in childhood, and since it is often a special problem of the ophthalmologist we shall describe it in detail.

CASE REPORT

Name—R. R.
Age—Two years
Sex—Female
Place of birth—San Pedro, Sonora
Weight—21.12 pounds.
Height—30 inches

PRESENT HISTORY

This child was first seen in our ophthalmological clinic last August. The parents of this child first noticed slight exophthalmos of the left eye, which had been getting worse day by day. After one month of these symptoms a progressive swelling appeared on both temporal regions. Last September the child was operated upon in Navojoa. Three upper teeth extractions were performed with possible curettage

of the maxillar sinus. Penicillin and streptomycin were then injected.

PAST HISTORY

The child was born normal with no pathological data at all.

PHYSICAL EXAMINATION

A very under-nourished child, with slight greenish palor. The skin is dry with very little elasticity. Temperature, normal. Upon examination, the child offers no resistance, being completely indifferent to his surroundings. Physical examination shows a great exophthalmus and chemosis of the left bulbar conjunctiva that protudes over the left eyelid. The eyelashes are covered with mucopurulent secretion. There is a ptosis of the upper lid. The eye appears to be pushed upwards. The conjunctiva is slightly-pale and the cornea has some changes in its transparency. There is slight anisocoria due to midriasis of the left eye where the photomotor reflex is slow. In the right upper eyelid there is a tumor mass, whose consistence is very hard (bone?) which appears to be continuous with the bones of the orbit. In the lower right eyelid there is another but smaller tumor similar to the one described above. All around the eye the color of the skin is slightly violet with increased vascularization.

Hypertelorism—(interpupillary measurement) 80 mms.



The tarsal and bulbar conjunctiva of the right eye is extremely pale with red hemorrhagic spots.

The fundus examination shows the optic disk to be of normal form and size but pale in color, and its borders are blurred and indistinct, especially in the left eye which is also edematous. The retinal vessels are enlarged and tortuous. His face has a frog-like appearance and upon touching all these growths they have a bone-like hardness. The root of the nose appears to be caved in. The mouth is constantly open. The lips are pale and the two upper left molars are gone, also the second upper right molar. The head is normal in size and the bones of the skull appear to be separated. There is also another growth in the left submaxillary region. This tumor also appears to be very hard, not painful and apparently is a part of the maxillary bone. This growth has the size of a nut, and has increased accessory vascularization. All the nodes of the carotid and submaxillary regions are palpable. The chest is normal. The abdomen is enlarged with an umbilical hernia. The liver is enlarged 4 cms. below costal border, not painful. There is slight pre-tibial and maleolar edema. Both the inguinal and axillary nodes are palpable. The child appears slightly subnormal in intelligence.

The X-ray (Waters' position) show the existence of large condensations in both orbits, especially in the left side giving the aspect of bony growths. In the A.P. film the skull union

sutures are quite separated with increased osseous condensation in the fronto-parietal-temporal regions. In the left lateral film the separation of the skull sutures mentioned above are more noticeable.

LABORATORY FINDINGS

Kahn-Kline—Negative

Blood type—"O"—Rh. Negative

T.B. test—1x1000—Negative.

Blood cell count—

Red cell—950,000—Hemoglobin—4.30 grms.

White cells—413,000—Basophiles—0—Eosinophiles—0

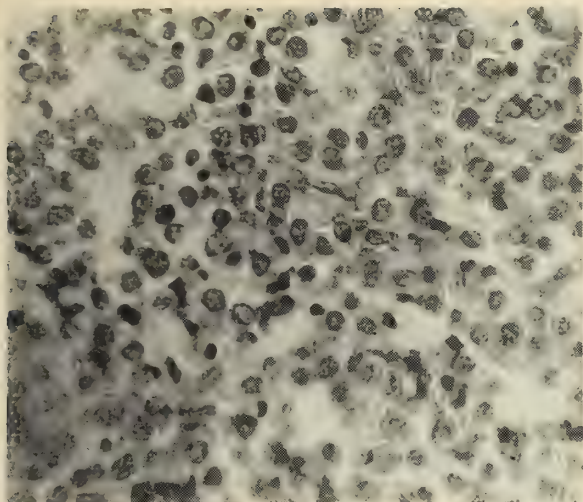
Undifferentiated forms—Monocytic series—59

Juveniles—2 Segmented—2 Lymphocytes—26

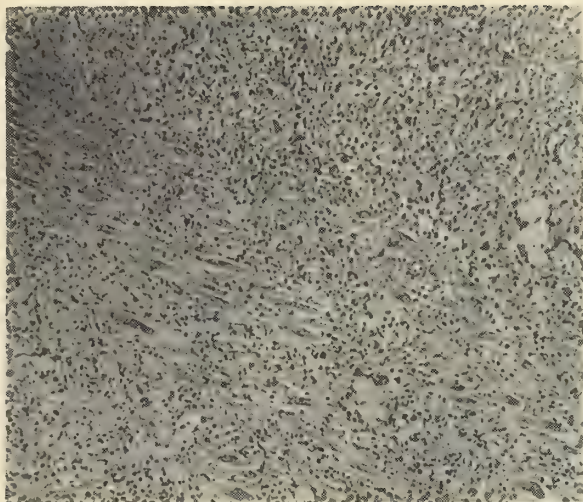
Monocytes—10

Auer's bodies in the undifferentiated series.

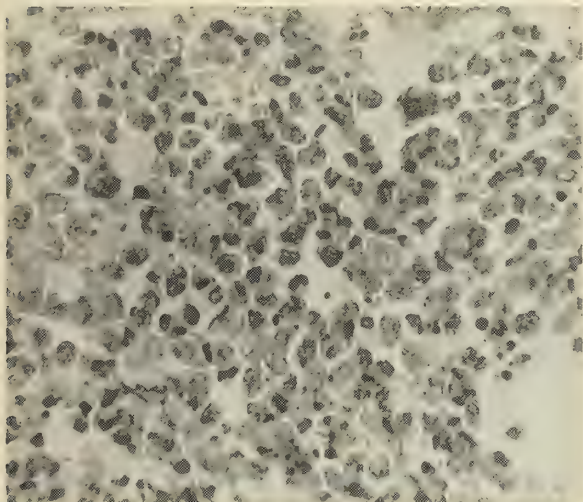
PATHOLOGY—A Lymph node was taken from the neck on October 16. It was a moderately enlarged node, slightly hard; the cut surface showed a uniform gray-yellowish tissue, somewhat congested. The specimen was fixed in Bouin's fluid and frozen sections were made. Microscopically the sections showed a complete loss of the normal architecture and only a few lymphocytes could be seen; the rest of the section was formed by sheets of free round cells, larger than lymphocytes, with vesicular, oval or kidney-shaped nuclei containing one to three nucleoli. Typical and atypical mitosis were frequent. These findings were thought to be consistent with leukemia or reticulum cell sarcoma.



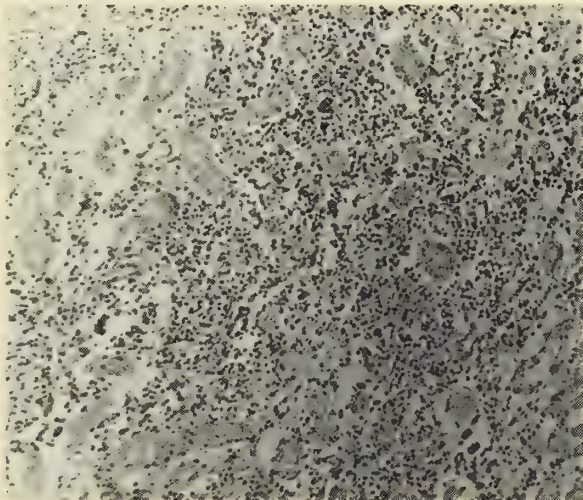
Section of Lymph Node.—Most of the cells are very young leucocytes with vesicular nucleus and several nucleoli. There are some normoblasts.



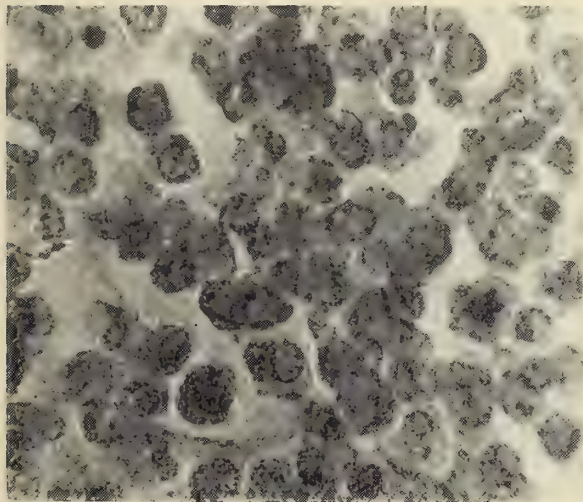
Section of the Temporal Mass.—There are some muscular fibers scattered among the Tumor cells.



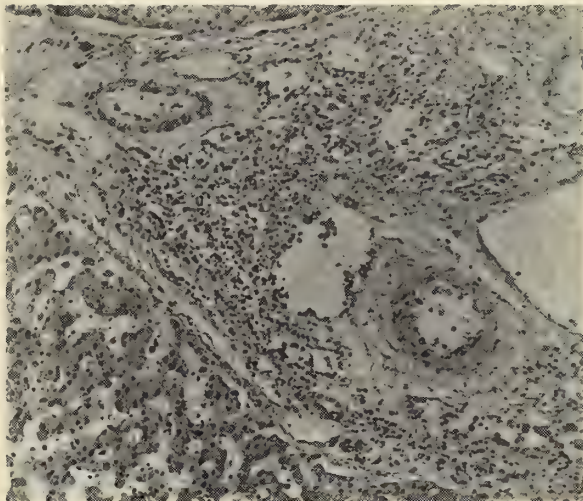
High power of the Tumor in post mortem material.—Most of the cells are blast blood cells; there are small foci of erythropoiesis.



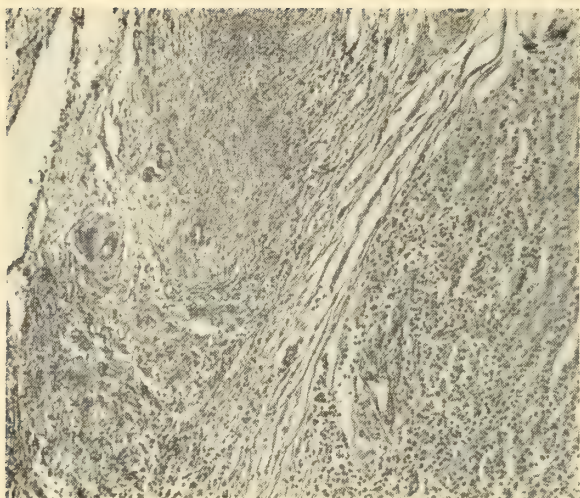
Infiltration by Tumor cells in the Cortex of the Kidney.



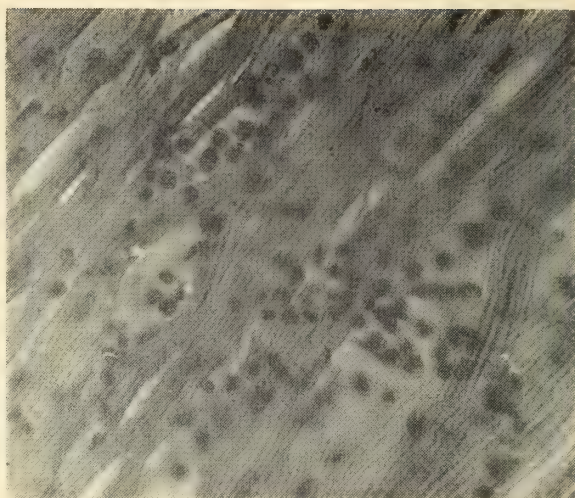
High power (immersion) of the Tumor cells.—There is a mitotic figure in one of them.



Section of the Liver.—The portal space shows a dense infiltrate by Leukemia cells. The sinusoids are moderately dilated and the Kupffer cells are conspicuous.



Section of the Right Lung.—The left side shows a tuberculous area with caseation and Laughan's cells: The right side is a hilar region infiltrated by Leukemia cells.



Infiltration by Tumor cells in the Myocardium.

Studies in the peripheral blood disclosed an extreme anemia (950,000 R.B.C.) and a very high white count (413,000) with 59% of blast forms, many of them containing Auer's bodies.

A specimen taken from the sternum gave a scanty grayish material which stained by Wright's method, showed also a very high percentage of blast undifferentiated cells (hemocytoblasts).

The patient died on November 2, and a complete autopsy was performed. There was extreme anemia in all the organs. The tumor masses of the orbit and temporal regions, on cut sections, showed a firm, bright-green tissue one to three cm. thick. Invasion by this tumoral tissue was found in the following organs and regions; tonsils and pharynx, cervical and mesenteric lymph nodes, both lungs in the form of miliary nodules or green patches in the hilar regions, both kidneys had extensive greenish cortical and medullary areas, the liver did not have limited green periportal areas; all along the anterior aspect of the vertebral bodies, the costovertebral junctions, and the internal aspect of the ribs; this invasion was a uniform one to three mm. continuous layer; however, several actual nodules were seen; in the dura mater as flat nodules; one of them located over the Torcular herophili obstructing partially the venous circulation; finally, the same green tissue was found all along the separated cranial sutures.

Contrary to what all the text books say, the bright "jade" green color of the tumor did not

fade on contact with the air or in the fixative (formaline). Ten days later, the color was as bright as in the first day.

Other findings were petechial hemorrhages in both lungs and the myocardium, and a semicalcified subpleural nodule in the right lung, with it corresponding hilar node, moderately enlarged.

Microscopically, the tumor tissue from the temporal masses, shows a dense infiltrate of free round cells in an abundant adult stroma.

Under high power, there is a mixed infiltrate which recalls that of "Mycosis fungoides"; however, the predominant type of cell is a very immature blood cell; there are also numerous foci of erythropoiesis. The infiltrate of the several viscera, is identical in all sites. The tonsils and the spleen show all the medullary spaces and sinuses filled by blast cells without forming real nodules. The bone marrow is very poor and the normal blood forming tissue is almost lost. The pulmonary node and the hilar lymph node show typical tubercles and caseation.

SUMMARY—A characteristic histological picture of leukemia is found in this study. Although upon the surgical biopsy specimen and the peripheral blood picture it was thought to be a monocytic type of leukemia, in the postmortem material this could not be supported and the final impression is that it is a case of acute leukemia, undifferentiated. A typical "chloroma" syndrome developed associated with leukemia. A primary tuberculous lesion was developing in the right lung.

TREATMENT OF BURSITIS WITH INTRAVENOUS IRON CACODYLATE

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Bursitis is an inflammation of those serious-lined compartments placed here and there throughout the body where friction between the overlying soft parts and closely related firm parts is most apt to be extreme. Therefore, bursitis is a broad term covering a large number of painful and disabling situations. It arises frequently in general practice and may well form a significant part of the practice of the rheumatologist.

Its recognition may be quite simple. On the other hand, ileopectineal bursitis for example may present a definite problem from the diagnostic standpoint. Its possibility must always be kept prominent in the differential diagnosis in disturbances in the regions of joints and in areas of pain and tenderness far removed from the articular structures.

The diagnosis of bursitis is based on:

1. Pain, usually severe and agonizing in the region of the joint. The patient often volunteers that the pain seems more in the muscle than in the joint.

2. Radiation of the pain, often simulates that of neuritis. When the subdeltoid is involved the pain may radiate into the neck, arm, insertion of the deltoid, forearm and even to the finger tips.

3. The limitation of motion may be marked, due to the pain. The pain is extreme in acute cases with the slightest attempt at motion.

4. Tenderness over the involved area such as the sacro-iliac joint; or in the case of a subdeltoid bursitis, in the region of the greater tuberosity of the humerus just below the acromial process (and at times over the entire shoulder). The coracoid process and bicipital groove may also be sensitive to pressure. Often the point of greatest tenderness is over the deltoid insertion.

5. A mass or swelling may be present. In the peripheral joints especially the knee or elbow the bursal effusion may be tremendous. In the case of a subdeltoid bursitis a mass may be palpable over the deltoid insertion and this is usually the point of maximum tenderness.

6. Local heat may be present.

7. Roentgenograms may demonstrate calcium deposition in the involved bursa or tendons.

8. Usually a single bursa is involved, although not infrequently a bilateral subdeltoid bursitis is encountered.

9. A history of trauma, sometimes seemingly extremely mild, or exposure to cold or drafts may often be elicited.

When it is known, according to Comroe (1) that the approximate frequency of causes of a painful shoulder is a subdeltoid or subacromial bursitis in at least 80 per cent of all cases, one seems justified in treating this painful joint as a bursitis, until proven otherwise. If there is the slightest suspicion of a painful joint being due to bursitis, it is our policy to institute treatment immediately for bursitis.

Bursae are extremely numerous throughout the body. Indeed Virchow (2) claimed to have dissected in the neighborhood of 70 in the region of the knee joint. The number of bursae about the body is inconstant. They are formed whenever a need for them arises in response to chronic irritation of a sliding or rubbing motion. The connective tissue (3) apparently has the ability to undergo change under adequate stimulation to form the endothelial type of lining of the bursae.

The economic importance of bursitis is not inconsiderable. The baseball pitcher who develops a "glass arm" may have to leave a remunerative occupation and confine his activities to one which puts less strain on the rotators of the shoulder. The stenographer may have to be off work for a long period of time until abduction of the arm can be maintained without pain. The end result of a chronic subdeltoid bursitis—the "frozen shoulder" is only too well known and one can conceive without difficulty the economic liability of such a member. Successful treatment of bursitis, then, becomes important. It is important primarily from the standpoint of relief of an intense or nagging pain and restoration of normal function. It may be a factor in the patient's personal economy, since many of these disabilities arise as a result of an occupation.

The methods of treatment of bursitis are several, regardless of the stage of the disease. The

choice of treatment usually depends upon the stage of the bursitis, the facilities at hand, and the training or specialty of the physician. It seems in order to place here the statement on treatment made by the committee of the American Rheumatism Association in its Primer on Rheumatic Diseases published in the Journal of the A.M.A. last year:

"Treatment (of bursitis) (4) should be directed to relieving the pain, maintaining function and reassuring the patient as to the relatively mild nature of the disease. Local application of radiant heat or diathermy may relieve, but often aggravates the pain, in which case cold usually relieves. Rest during the more acute phase followed by graded exercises to restore motion is helpful. Withdrawal of exudate from a distended burse promptly relieves. Local roentgen therapy helps in some cases, especially in the subacute stage. Local procain infiltration of brachial plexus or superior cervical ganglion block will usually give temporary relief, which in addition to providing analgesia will allow exercises to maintain motion of the affected shoulder. If calcification is firm and adhesions restrict motion, excision of the calcific mass and liberation of the shoulder may be required.

"With proper care promptly provided, acute bursitis can usually be arrested or controlled. If it becomes chronic, periarticular fibrositis may result and enhance the shoulder disability. If stiffness of the shoulders persists, muscles atrophy and motion becomes so limited that a "frozen shoulder" may result. Careful manipulation with the patient under anesthesia may be required to regain motion."

It is not the purpose of this paper to enter upon a critical discussion of the merits of the multiple puncture, through-and-through irrigation, novocaine injection, the various modalities of physical therapy, of x-ray, or surgical excision. Rather it is an attempt to re-emphasize the value of the cacodylates, and specifically, iron cacodylate, in the treatment of the non-specific type of bursitis and to re-enter this drug into the therapeutic battery of the physician as practical, inexpensive, available and satisfactory.

Pharmacology: To date, it must be stated that iron cacodylate is used empirically. Satisfactory pharmacologic evidence as to its mode of action is lacking.

The cacodylates are one of the group of organic pentavalent compounds of arsenic. They

are reported (5) to slowly liberate inorganic arsenic into the body. The action on tissue cells is considered likely to be (6) that arsenic compounds may react with the sulfhydryl (SH) grouping in cells and in this way interfere with cellular oxidation. Dustin (7) in 1930 has shown that sodium cacodylate can arrest mitosis and produce nuclear abnormalities. Arsenic (8) also inhibits cellular enzymes, as for example nuclease and phosphatase. About one third of a single dose of sodium cacodylate is eliminated in 24 hours, and traces (9) may appear for as long as 4 weeks.

It should be stated here that from our experience in giving several thousand injections, no symptoms or physical signs of toxicity have occurred with the exception of nausea in occasional patients. This has been borne out in the experience of others who have used this agent in the treatment of the condition in question.

Apparently, the earliest published report of the use of iron cacodylate in the treatment of bursitis is that of T. K. Richards in the New England Journal of Medicine in 1931 (10). Dr. Richards was treating a chemist for boils by injections of iron cacodylate. The chemist had a "mildly inflamed subacromial bursa" and began to report that the shoulder improved with each injection. This observation led to trial on other patients with equally good effect, with the result that he published his experience in a small series of cases treated by this method.

A surgeon, Dr. Thew Wright, Emeritus Professor of Surgery of the University of Buffalo School of Medicine, treated a substantial number of cases of bursitis with iron cacodylate satisfactorily and introduced the method to one of us. (C. E. B.) It has been used by us for over a period of some ten years.

The only other published report which has been found is that of Dr. Louis Perner which appeared in Industrial Medicine in 1944 (11). In this report, a series of 75 cases were treated and it was the author's statement that "the results were invariably good when the condition was present for several days to several weeks." So impressed was Dr. Perner, that he felt the drug might be used as a diagnostic measure. He attempted to explore the mode of action and found that addition of iron cacodylate to whole blood inhibited or prevented clot retraction, whereas another iron salt produced no inhibition and sodium cacodylate produced

much less inhibition of clot retraction. He concluded that the essential mode of action of iron cacodylate was unknown but that it appeared to be due to a physico-chemical change in the blood.

It has been our practice to use iron cacodylate alone usually, (except for appropriate exercises) or in conjunction with some form of physical therapy.

The preparation of iron cacodylate used is a 3% aqueous solution. Five cubic centimeters are administered slowly by intravenous injection. It is usually given daily until there is a favorable response, then every other day. The total number of injections varies with the response of the individual patient.

In the analysis of 100 attacks of bursitis, there was a distribution of 37 males and 63 females. This report includes two or more attacks in the same individuals in 13 patients, (7 females and 6 males), a total of 35 attacks. The youngest patient was a 19 year old female, and the oldest patients were an 84 year old female and an 84 year old male. Both suffered an acute attack of bursitis of the knee. Most of all these 100 attacks of bursitis were associated with a definite history of trauma (sometimes what seemed very minor) or exposure to cold. This latter was especially true of the bursitis involving the shoulder. In the Spring and Fall, with warm days and cool nights, we found several cases occurring in men who slept without pajama tops; the shoulder being exposed to the cold air during heavy sleep. We have come to expect several attacks of bursitis of the shoulder each Spring and Fall. The left shoulder seems more prone to attacks, possibly because this shoulder is exposed to drafts in driving with the car window open.

The average age of the patients was 49.5 years. There seemed no age which seemed immune to attacks of bursitis. While the preponderance of our cases were in females, this series is too small to be of significance. We did gain the impression that some people seemed to be more susceptible to recurring attacks, but for this we were unable to account for any common factor.

This was the initial attack in 57 cases, some of these reported cases have been under observation for five years and have developed subsequent attacks varying from one to three.

The shoulder was involved in 51 cases, various other joints in decreasing frequency were

sacro-iliac, knee, elbow, wrist, etc.

The average number of treatments necessary were 9.2. The average number of treatments necessary for relief were 2.8. By relief is meant that the patient was made to resume his normal occupation without resorting to medication for pain of any type. At the end of the treatment, 80 patients or 80% were reported as well. By this is meant that the patient had been entirely free of pain for at least 72 hours and had no resulting limitation of motion. Patients were classified as improved even if they only had an occasional twinge of pain or any limitation of motion, even though the motion may have improved to a marked degree. There were 19 cases or 19% which showed improvement. This group includes 4 patients who received five to eight injections but discontinued treatment usually because of leaving town. There was one failure; a female who received six injections and showed no improvement and refused further treatment. We have one other case we consider a definite failure with iron cacodylate. This patient was not reported in this series because he was not one of the last 100 cases. This man was sent to Tucson from Detroit with the supposed diagnosis of rheumatoid arthritis of some four to six months duration but he had a very definite subdeltoid bursitis. He received 12 injections with only very minor relief and subsequently cleared entirely after x-ray therapy.

The patients were grouped according to the time elapsing between onset of symptoms and the start of treatment as follows:

1st: One to three days. These patients were usually in excruciating pain and therefore they sought help early. They required an average of 6.6 injections for complete recovery, with an average of 2.6 injections for relief. There were 28 patients in this group with 25 complete recoveries. Of the three patients reported as improved, one received seven injections, and another only four injections.

2nd: Patients who waited four to seven days required an average of 9.2 injections for complete recovery with 3.4 injections for relief. There were 20 patients in this group, 18 showing complete recovery, and two as improved. Again one of the improved left town after the 4th injection.

3rd: Patients who first sought help eight to thirty days after onset of their symptoms required an average of 9.6 injections for recovery.

There were 19 patients in this group, 17 recovered completely, one showed improvement, and there was one failure (the patient reported above who after receiving six injections refused further treatment).

4th: Those who had their disability from thirty-one days to a year required 11.6 injections and in this last group the percentage of complete recovery was only 63% with the remainder showing only improvement varying from marked to moderate whereas the group seeking relief in the first three days showed a percentage of 89.3% who recovered entirely.

This would tend to point out the fact that the earlier treatment is instituted the higher the percentage of complete relief is encountered and the fewer injections is required. Some of the patients in this group classified as improved received only four or five injections but were classified only as improved since when they were last seen they were not 100% recovered.

In selecting the following case reports, those cases which had no treatment except for intravenous injections of iron cacodylate are reported.

Mrs. R. B. W., aged 46 years was first seen June 2, 1944, complaining of pain in the left shoulder of two days duration. The pain was steady, with sharp pain on attempting motion, seeming to "run way down to the wrist". The patient carried her arm in a sling. She had applied heat with slight relief but did not get much sleep. Examination showed no fever. There was marked tenderness over the tip of the left shoulder and over the entire deltoid area. The slightest attempt at motion in the shoulder especially abduction or rotation, caused excruciating pain. She was given five cu. cms. of a three per cent solution of iron cacodylate intravenously. The following day she was able to drive her own car to the clinic. Thereafter she was given three more injections on alternate days. On the third visit she volunteered that she was very much improved. On her last visit, she was free of pain but never the less was given her fifth injection of iron cacodylate. On attempting to find a cause of this attack, the patient was asked if she had been exposed to any drafts. She stated she had sat in the breeze of a window cooler reading a book. Two years later she was again seen complaining of pain in the left shoulder which she had first noticed the preceding day on leaving an air conditioned movie. She was given three injections of iron

cacodylate on three successive days with complete relief. She returned 14 days later stating she now had bursitis in her right shoulder although the pain was not as severe as with her previous attacks. She again was given four injections of iron cacodylate on successive days. On her fourth visit she stated she had had no pain for 24 hours and the morning of her last visit she had done the family washing before coming to the clinic for her injection. She has had no subsequent attacks during the past four years.

Mrs. B. O. B., aged 52 years was first seen because of severe pain in the lower back. The patient stated the pain had started suddenly just after lunch the preceding day. The pain was so severe she was unable to turn over in bed without assistance, and with assistance she screamed with pain. She stated that two years previously, she had had a similar attack and was hospitalized for two weeks. Examination showed marked tenderness over the left sacroiliac joint. There was considerable muscle spasm of the lower back, more marked on the left. She was given seven injections intravenously of iron cacodylate. The second day the pain was much less acute, and the following day the patient was up and around with only an occasional twinge. She volunteered that if her car had been available she could have driven to the clinic. She came to the clinic for four subsequent injections on alternate days. On her last visit she stated she had been entirely free of pain for 48 hours. She was discharged as recovered.

Mr. R. B., an 84 year old male, was seen because of acute pain in the right knee. The previous day he had been on his hands and knees weeding his lawn and had noticed slight pain in the right knee towards evening. This became worse during the night and by the next morning it was so intense that the patient was unable to move without screaming with pain. He had his knee propped up and flexed on pillows. There was a tremendous fluctuating swelling of the right knee, with very definite increase in skin temperature. The swelling seemed due to effusion into the suprapatellar bursa. It did not seem possible that iron cacodylate could be effective in causing the absorption of this amount of fluid, and it was thought it would be necessary to aspirate the bursa. Nothing was done except for intravenous iron cacodylate on four succes-

sive days. Within 24 hours the patient was more comfortable and by the fourth day was able to walk, although he had some pain on walking. He was given six more injections on alternate days and by the tenth injection was entirely comfortable and the bursal effusion had entirely absorbed. This old gentleman lived to be 90 years of age and had no subsequent attacks.

In summary, we have reported 100 unselected cases of bursitis (acute, subacute, and chronic) which were treated with intravenous iron cacodylate and in some instances with accompanying appropriate physical therapy. Of these 100

cases, 80% were reported as recovered, 19% as improved, and 1% as a failure.

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THE EFFECT OF CONCENTRATION OF SERA ON THE SEROLOGICAL TESTS FOR SYPHILIS

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The present day concept of syphilis serology states that there is an antibody-like substance in the blood stream (reagin) that reacts with the antigen, causing it to produce a floc, and fix complemen (1). This theory presumes that there are demonstrable antibodies in the blood stream of the syphilitic, but does not explain zone reactions in known syphilitics, nor why normal individuals will at times give positive serological tests. Furthermore, it does not offer any explanation why diseases other than syphilis will flocculate the antigen or fix complement.

Previous work by the authors (2, 3, 4) has indicated that the production of a floc by any sera was due to the divalent cations in the sera replacing the monovalent cations on the antigen and thereby flocculating the suspension. Consequently, concentration of negative sera by dialysis through a semi-permeable membrane should produce a positive test. Also, simple concentration by evaporation would not be expected to alter the seroactivity of any sample. This should be true because in the case of the dialysed sample there would be an unbalancing of the normal ionic content in the sera while in the second case the proportions remained constant. In order to study the relative effects of concentration by dialysis and evaporation the following experiments were carried out:

Blood samples as they were received by the laboratory were separated from their clot and

centrifuged for five minutes and the clear sera poured off. Standard Klines, Hintons, and Kahns (diagnostic) were run on all sera. Only clear, unhemolyzed sera were used in these experiments. The sera were then pooled according to their reactivity, and again checked by the Kline method. Negative, two plus and four plus sera were saved until a total of 130 ml. were obtained of each reaction. These pooled sera were then divided into two 65 ml. portions, A and B.

Portion A was placed in a porcelain evaporating dish and an electric fan placed so as to blow a stream of air over the surface of the sample. In this way the sera were completely dry within 45-60 minutes at room temperature. The dry powder was carefully ground in an agate mortar, and placed in a screw-capped homeopathic vial until ready for use. This powder was dissolved in 30 ml. of distilled water, giving a solution containing a little over twice as many solids as were contained in the original 65 ml. sample of serum. Serial dilutions were then made on this suspension. Standard Klines, Hintons, Kahns and Kolmer Wassermanns were run on each dilution. The results are given in Table I. The concentration is expressed as the percent of concentration of solids, (65 ml. being taken as 100%), since the dried sera were obtained from pooled sera of that volume. Ten samples of pooled sera were run on each reaction, (Negative, 2+ and 4+). Only the re-

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TABLE I
The Effect of Serum Concentration on Sero-activity

		KAHN			KLINE			HINTON			WASSERMANN		
% Serum Concentration*		Neg.	2+	4+	Neg.	2+	4+	Neg.	Pos.	Pos.	Neg.	2+	4+
229%	Reaction	-	2+	4+	-	2+	4+	-	+	+	-	2+	4+
	Titre	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128
162%	Reaction	-	2+	4+	-	2+	4+	-	+	+	-	2+	4+
	Titre	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128
130%	Reaction	-	2+	4+	-	2+	4+	-	+	+	-	2+	4+
	Titre	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128
100%	Reaction	-	2+	4+	-	2+	4+	-	+	+	-	2+	4+
	Titre	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128
93%	Reaction	-	2+	4+	-	2+	4+	-	+	+	-	2+	3+
	Titre	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128	-	1-8	1-128
81%	Reaction	-	2+	4+	-	2+	4+	-	+	+	-	1+	3+
	Titre	-	1-4	1-64	-	1-4	1-64	-	1-4	1-64	-	1-1	1-32
65%	Reaction	-	1+	4+	-	1+	4+	-	+	+	-	-	3+
	Titre	-	1-2	1-64	-	1-2	1-32	-	1-2	1-32	-	-	1-32
56%	Reaction	-	-	4+	-	-	4+	-	+	+	-	-	3+
	Titre	-	-	1-32	-	-	1-32	-	1-2	1-16	-	-	1-16
52%	Reaction	-	-	3+	-	-	4+	-	-	+	-	-	2+
	Titre	-	-	1-32	-	-	1-32	-	-	1-16	-	-	1-4
50%	Reaction	-	-	3+	-	-	3+	-	-	+	-	-	2+
	Titre	-	-	1-32	-	-	1-16	-	-	1-16	-	-	1-8
46%	Reaction	-	-	2+	-	-	2+	-	-	+	-	-	2+
	Titre	-	-	1-4	-	-	1-4	-	-	1-4	-	-	1-4

sults of one representative sample from each will be given.

Portion B was concentrated by dialysis through a cellophane tube. A length of cellophane dialysing tube (1½ Meter) similar to those used in transfusion sets, was attached to a 50 ml. burette and the open end closed off by means of a pinch clamp. The sera were poured into the burette, the cellophane tube allowed to fill, and a stream of air directed against the tube. As the sera dialysed through the tube the number of milliliters loss could be determined by reading the drop on the burette.

When the sera had lost 40% by volume they were drawn out, thoroughly mixed and a 3 ml. sample removed. Sample 1—The burette and tube were washed and with double distilled water in sufficient quantity to add to the concentrated sera and make them back up to volume, and a second 3 ml. sample removed

(Sample 2). For example, for an original 100 ml. sample concentrated to 60 ml. 40 ml. of double distilled water was run through the burette into the 60 ml. of concentrate. In this way the volume of sample was the same as the original control sample. However, the total salt concentration had decreased since the smaller ions would diffuse, or dialyse, through the permeable membrane at a more rapid rate than would the larger protein and lipoidal molecules would. Sodium and potassium would pass through the membrane much more rapidly than the larger more highly charged calcium molecule. After sample 2 was removed the cellophane dialysing tube was placed in the sera and thoroughly shaken in order to dissolve any ions that had dialysed through the tube. Another sample was then removed (sample 3). The last step was performed with the thought that the dialysed salts when added back to the sample (sample

TABLE II
Effect of Concentration by Dialysis on Sero-Activity

	KAHN			KLINE			HINTON			WASSERMANN		
Control Sample Titre	Neg. -	2+ 1-8	4+ 1-128	Neg. -	2+ 1-8	4+ 1-128	Neg. -	2+ 1-8	4+ 1-128	Neg. -	2+ 1-8	4+ 1-128
Concentrated to 60% of volume Titre (1)	4+ 1-256	4+ 1-512	4+ 1-1024	4+ 1-256	4+ 1-512	4+ 1-1024	Pos. 1-256	Pos. 1-272	Pos. 1-1024	3+ 1-64	4+ 1-512	4+ 1-1024
Made up to original volume with dis- tilled water Titre (2)	3+ 1-128	4+ 1-256	4+ 1-512	3+ 1-256	4+ 1-256	4+ 1-512	Pos. 1-256	Pos. 1-256	Pos. 1-512	2+ 1-16	4+ 1-128	4+ 1-256
Cellophane tube added Titre (3)	Neg. -	2+ 1-8	4+ 1-128	Neg. -	2+ 1-8	4+ 1-128	Neg. -	Pos. 1-8	Pos. 1-128	Neg. -	2+ 1-8	4+ 1-128

2) should neutralize or offset the effect of concentration and dialyses. All three samples were heated at 56°C. for 30 minutes and examined by the same four tests as given above. The results are given in Table II. Ten samples were run at each concentration (Negative, 2+, and 4+), but only one representative sample of each are given in the table.

DISCUSSION

If we are to accept the present day concept of an antibody like substance in the blood stream of syphilitics (reagin) it would necessarily follow that simple concentration of the total solids dissolved matter in the sera would result in the production of a positive test. If, however, we assume that the reactivity of any given sera is due to the preponderance of one normal constituent over another ($\text{Ca}^{++}:\text{Na}^{+}$)—that is, an upset ionic ratio—mere concentration of serum solids would not effect the sero-activity. Table 1 demonstrates this point very clearly. Even when a given sera contained over twice the normal solids (239%) the reactivity was not altered.

Likewise, if the reactive substance is a large molecule, (lipoid,) as it is presumed to be, we would expect to increase the reactivity, or titre, when the sera were concentrated by evaporation and when the concentrated sera were again made up to their original volume with distilled water it would be expected that the sample would return to its normal control reaction. We failed to obtain these results in our experiments. If, however, the reactivity were due to an upset in the ionic balance in the sera we would expect that (a) on concentration by dialysis or diffusion, any sera should become

more strongly sero-active, (b) that when these sera were made up to volume with distilled water little or no change should take place in their titre, and (c) that if the tube used for dialysis were washed with the diluted sera that that dialysed material should go back into solution and restore the sample to the control reaction. This point was illustrated in Table II.

From the data presented in this paper it would appear that the active ingredients in any sero-active serum is some normal constituent that has become dominant due to an actual increase of that element or the decrease in some other portion. Previous work in this laboratory has indicated that the divalent cations of Ca^{++} and Mg^{++} (lit. cit.) are responsible for the production of the floc in the various tests. When sera are concentrated by evaporation the monovalent: divalent ratio is not disturbed, even though there is an increased per unit volume, therefore there is no appreciable increase of Ca^{++} over Na^{+} ; on the other hand Na^{+} will pass through a semi-permeable membrane much more rapidly than will the larger, more highly charged Ca^{++} , thereby upsetting the normal balance in the sera. With the relative increase of the Ca^{++} there will be more divalent cations to react with the zeolite-like indicator, replacing the Na^{++} on the molecule and thereby forming a floc and a positive test. When the dialysed sera were made up to volume with distilled water the $\text{Na}^{+}:\text{Ca}^{++}$ ratios were not changed, therefore, what little effect there was noted was due to a dilution factor. The addition of the dialysing tube, however, replaced the lost ions of Na and restored the normal $\text{Na}^{+}:\text{Ca}^{++}$ balance for that sample and thereby returning the serum to its normal reaction.

CONCLUSION

1. Concentration of sera by evaporation will not alter the sero-activity of that specimen.
2. Dialysis of a serum through a semi-permeable membrane will result in a positive reaction to the various tests.
3. Dialysed sera when made up to volume with distilled water do not return to their normal titre.
4. The addition of the dialysed material by washing the dialysing tube in the diluted sera

results in a decrease in titre and return to its control reaction.

5. The results indicate that the ionic balance, probably $\text{Ca}:\text{Na}$, is responsible for the reactivity of any given serum.

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BASIC SCIENCE SEMINAR

DRUGS AFFECTING THE AUTONOMIC NERVOUS SYSTEM

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INTRODUCTION

A subject of considerable recent medical interest, both in the laboratory and clinically, is the actions and uses of various groups of drugs affecting the autonomic nervous system. For a discussion of these drugs it is necessary first to consider briefly the structure, function and nomenclature of this nervous system.

All structures of the body aside from the skeletal muscles are supplied by fibers of the autonomic nervous system, both efferent and afferent. The main characteristic of these structures, and that responsible for the name of the system, is that of automatic action following nerve section. The afferent fibers are quite similar to sensory somatic fibers, both in structure and in reaction to drugs. The efferent fibers are divided into the two main categories of sympathetic and para-sympathetic, usually with contrasting functions.

The fibers of both structures have one ganglia only between their issuance from the central nervous system and their termination in the end-organ. The sympathetic system has ganglia in three sites, vertebral; pre-vertebral; and terminal. The para-sympathetic usually has only terminal ganglia. In the sympathetic system the single synapse may occur in any of the ganglia

mentioned, and need not correspond to the level of chord origin. The sympathetic ganglionic fibers synapse with many post-ganglionic ones, the ratio sometimes being as high as 1:20. In contrast the fibers of the para-sympathetic system synapse in a much lower ratio, frequently being 1:1. Thus the sympathetic system tends to discharge as a unit while the discharge of the para-sympathetic is apt to be localized and selective.

Transmission of impulses is accomplished in effector organs by chemical mediation. It has been postulated that the type of reaction occurring (stimulation or inhibition) will depend on a substance in the organ. This is thought to combine with the chemical liberated at the nerve ending, which is acetyl-choline in the case of the para-sympathetic system and sympathin in nerves of sympathetic origin. Both substances are broken down by enzymes, cholinesterase and amine oxidase respectively. The action is very rapid with cholinesterase, but considerably slower in the case of amine oxidase, a point of clinical significance.

Transmission in ganglia is also accomplished by chemical mediators. On stimulation of pre-ganglionic nerves acetyl-choline is the chemical mediator in both sympathetic and para-sympathetic ganglia. The cells of the adrenal medulla are activated by pre-ganglionic sympathetic fibers, this anomaly being explained by the fact

that the cells are modified neuroblasts and homologous with sympathetic ganglion cells. Thus we have the phenomenon of acetyl-choline being the mediator of nerve impulses causing the release of epinephrine. Acetylcholine has two somewhat diverse actions, the so called muscarinic and nicotinic effects. The action usually attributed to acetylcholine (i. e. the transmission of impulses to effector organs) is the one classified as muscarinic, while the property of transmission of impulses at the ganglia (and stimulation of ganglia) is the nicotinic effect. This distinction is of importance when considering certain of the drugs affecting the cholinergic system.

For the purposes of this paper it would be advantageous to classify the portions of the autonomic nervous system on the basis of the chemical used as the transmitter of the nerve impulse. Using this as a guide we have all nerves classified under two headings—(1) cholinergic and—(2) adrenergic. The former includes not only all post-ganglionic parasympathetic fibers, but also all autonomic preganglionic nerves, whether sympathetic or para-sympathetic. In addition it includes the splanchnic nerves to the adrenal medulla. The latter includes those nerves which act through release of an epinephrine-like substance (adrenalin; sympathin). Thus these consist only of post-ganglionic fibers of the sympathetic nervous system.

The autonomic drugs act on cells and chemicals but not on nerve endings. The following is a sequence of events in the propagation of a nerve impulse. (1) Preganglionic nerve impulse—(2) Liberation of chemical mediator (acetylcholine)—in ganglia—(3) Post ganglionic impulse—(4) Liberation of chemical mediator at end-organ—(5) combination of mediator with receptive substance—(6) Specific Response of organ. Some drugs act at step number four, others at six, and still others facilitate step five. Drugs are much more effective on organs which have had their nerve supply interrupted. This is particularly noticeable in end-organs of adrenergic nerves. One clinical application of this is the well known fact that sympathectomies should be pre-ganglionic in location.

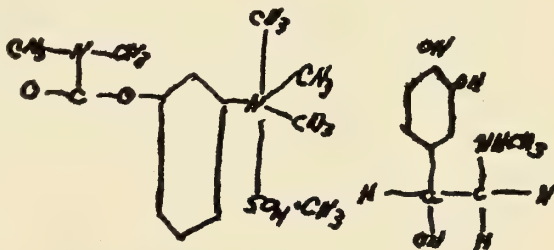
CHOLINERGIC DRUGS

A—Stimulatory

In this group we shall consider both those drugs having stimulatory and those having in-

hibitory effects on the cholinergic system. Among the former are Acetyl-B-Methylcholine, physostigmine, prostigmine, and pilocarpine.

Acetyl-B-Methylcholine (mecholyl) and *Carbaminoylcholine* were synthesized in an attempt to procure a drug having the properties of acetylcholine plus a degree of stability sufficient for clinical use. An additional property secured in these compounds was a lack of nicotinic effect. These drugs have various actions which would be expected to prove useful clinically, but which are in reality only rarely used. The most outstanding of these is that of contracture of the detrussor muscles of the urinary bladder. This action can be utilized in cases of chord bladders and in post-surgical urinary retention (dosage 20 mg hypo). Mecholyl has also found use in the treatment of paroxysmal auricular tachycardia, having been reported successful in 90% of cases (dosage 15-40 mg hypo). It is to be noted that this drug will not be effective in patients receiving quinidine. Still another field of usefulness is in lowering the blood pressure of essential hypertensives, (10 mg hypo) although this is not feasible for long management. Undesirable side actions consist of production of bronchial asthma in those susceptible, and occurrence of auricular fibrillation in hyperthyroid patients.



PHYSOSTIGMINE—PROSTIGMINE

Physostigmine and *Prostigmine* will be considered together, since they both contain the basic chemical structure for anti-cholinesterase activity, (methylearbaic ester group), and have similar actions. Their mode of action is by inhibition of cholinesterase, thus allowing a longer duration of action of acetylcholine at the nerve junction. This leads at times to bizarre effects, as these drugs thus act on sympathetic ganglia as well as on terminal para-sympathetic nerves, the total result depending on

the summation of effects. Both drugs act on the gastro-intestinal tract, increasing its tone and motility with resultant belching and defecation. This action finds use in the treatment of post-operative ileus, prostigmine being the drug of choice (0.25 mg hypo prophylactically and 0.5 to 1.0 mg therapeutically.) There is a similar increase in tonus of the urinary bladder (same dosage) which might prove of use in post-operative incontinence, and also in cases of tabes dorsalis. Physostigmine finds wide usage in the treatment of glaucoma because of the extreme miosis it produces, lasting from 24-48 hours, with resultant fall in intra-ocular pressure. Both drugs are of use in cases of myasthenia gravis, prostigmine, being the drug of choice because of the relative absence of miosis.

Pilocarpine, although producing somewhat the same results as physostigmine and prostigmine, acts by an entirely different manner. The site of action is the end organ itself, and action is independent of intactness of the nerve. All of the muscarinic, and none of the nicotinic effects of acetyl-choline are present. Its maximum effect is on sweat and salivary glands. Doses of 10 to 15 mg cause marked diaphoresis, sometimes amounting to 2 or 3 liters. This fluid will contain as much as eight grams of nitrogen in patients with an elevated non-protein nitrogen, but the danger of circulatory collapse is too great to permit this to be used as a form of therapy. This drug has been advocated in the therapy of atropine poisoning, but it does not combat the severe central manifestations of this condition. Its sole practical clinical use appears to be as a miotic, in which it is used in a 0.5 to 3.0% solution.

B—Inhibitory

Those drugs having an inhibitory action on the cholinergic system are atropine, scopolamine and trasentin. There are other members of the group, but these may be considered representative and of maximum clinical usefulness. The naturally occurring members of the group are a combination of an aromatic acid and complex organic bases.

Atropine and *Scopolamine* have both a central and peripheral field of action, atropine acting mainly in the latter and scopolamine in the former. Peripheral action occurs exclusively at the end-organ, there thus being no effect on the autonomic ganglia. The locus of action cen-

trally is unknown. The drugs are eliminated by hydrolysis and by kidney excretion.

The main structures affected are glands and smooth muscle, with inhibition of both. The effects on the salivary and sweat glands are particularly marked but of little clinical use. The main uses of atropine are to lessen motility and spasm of the gastro-intestinal tract, and as a mydriatic in cases of iritis. It is also of use pre-operatively to lessen the quantity of bronchial secretions. It is however of doubtful value in cases of colic, biliary or ureteral, and there is no appreciable action on gastric or pancreatic glands.

Scopolamine is primarily a central depressant. However, in large doses, or in individuals suffering pain it is apt to have an excitatory effect, with marked hallucination. This sedative and tranquilizing action is useful in the treatment of alcoholism and also as an adjunct to narcosis. Both scopolamine and atropine produce a moderate stimulation of respiration. Dosage of both is 0.3 to 0.5 mg. oral or hypo.

Trasentin is a synthetic member of the anticholinergic family, which acts directly on smooth muscle and does not seem to have the highly selective parasympatholytic action of atropine. Because of this trasentin can counteract direct muscle stimulants more effectively. It lacks the glandular and mydriatic effects of atropine and is thus more useful in certain conditions. It has long been successfully used in the treatment of peptic ulcers (75 to 150 mg. oral t.i.d.) but recently a new field of usefulness has been reported, that of aiding cervical dilatation in the 1st stage of labor. It is effectively used in cases wherein the cervical dilatation has remained static at four to five centimeters for several hours. Dosage is 250 to 400 mg, with delivery usually occurring within thirty minutes. A complication which must be watched for is a drop in blood pressure.

The most recent addition to the ante-cholinergic field is *Banthine* (methantheline bromide), which has been used with great success in the therapy of peptic ulcer. Its mode of action is the blocking of cholinesterase at effector organs and also at autonomic ganglia. The action at effector organs resembles atropine effect, but is of much longer duration. Its potency is such that it can actually cause complete cessation of all gastric motility, as determined by fluoroscopy with barium meal. It affects other organs

than the stomach, such actions being undesirable side-actions in the therapy of peptic ulcer. Chief among these is inhibition of the detrussor muscles of the bladder with incomplete voiding and stagnation of urine. There is also minimal drying of the mouth. Dosage is 50 to 100 mg three time a day and also in the middle of the night, the last mentioned dose being the most important. Its use is being evaluated in other diseases involving hyperactivity of the sympathetic nervous system, its action here being in the autonomic ganglia.

ADRENERGIC DRUGS

A—Stimulatory. Those drugs having a stimulatory effect on this system are best represented by epinephrine, and therefore we shall use this as an example of the entire group. In considering these drugs it must be remembered that stimulation of the sympathetic nervous system does not imply stimulation of all of the end organs innervated. Thus while increased sympathetic outflow results in stimulation of the nyocardium it also results in inhibition of gastro-intestinal motility. This must be remembered in considering the multiple actions of the adrenergic drugs.

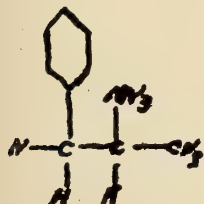
Epinephrine, a hormone closely related to the amino acid tyrosine, acts directly on effector cells. Since certain structures are stimulated and others inhibited by epinephrine, it is thought that there is a specific substance in the cells which determines whether the action shall be one of stimulation or of inhibition. The duration of action is dependent upon the rate of oxidation, amine oxidase taking part in its destruction. The many actions of epinephrine are too familiar to require discussion, but a brief list of those most characteristic might be of value. There is increase in blood pressure, contraction of the splenic capsula, bronchio-dilatation, relaxation of the gastro-intestinal tract,

stimulation of metabolism, and myocardial stimulation. There is no evidence of tachyphylaxis on repeated administration. Its main clinical use is in alleviation of acute attacks of bronchial asthma, in treatment of severe allergic reactions, and in prolonging action of local anesthetics. It is sometimes employed to control superficial bleeding, especially from the nasal mucosa.

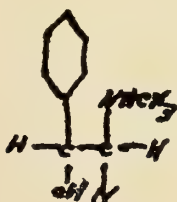
Ephedrine is an alkaloid, originally derived from a chinese herb. Its exact locus of action is unknown, but it has been postulated that it combines with amine oxidase, thus acting in much the same manner as physostigmine in the cholinergic system. Ephedrine is very similar to epinephrine in its actions, with certain notable exceptions. Ephedrine can be given by mouth and has a longer duration of action. It exhibits the phenomenon of tachyphylaxis, and stimulates the central nervous system. It is of benefit in myasthenia gravis and acts as a mydriatic otherwise it has somewhat the same field of usefulness as epinephrine. Its fate is unknown, but it is known that it is not destroyed by amine oxidase, and is not rapidly excreted by the kidneys.

Neo-synephrine is quite similar to ephedrine in chemical structure, being synthesized readily. Its actions also are similar to ephedrine with the exceptions of absence of tachyphylaxis and increased stability and duration of action. Side reactions of nervousness, tremor and headache are low. It finds its widest use in local vasoconstrictive action. It is also valuable for maintaining blood pressure in anesthesia (5 mg hypo repeated prn) and for therapy of orthostatic hypotension (25 mg oral three times each morning). It has little central stimulation.

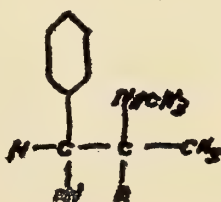
Benzedrine and *Dexedrine* are sympathomimetic amines very similar in structure and actions to ephedrine. However, the central actions are much more marked, forming the basis for the



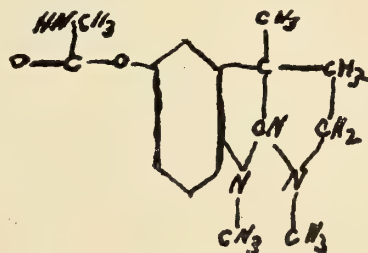
Epinephrine



Ephedrine



Benzedrine



Neo-Synephrine

clinical usefulness, while the peripheral actions are much less intense. The central actions consist of cortical stimulation, with euphoria, lessened fatigue, sleeplessness, enhanced ability to concentrate and increased motor activity. Because of these marked cerebral effects there has developed a considerable degree of habituation to this drug, especially in prisons and disciplinary barracks, where the problem has become quite serious. In these institutions the usual method of ingestion is oral administration of the contents of inhalers.

The purposes for which it is used clinically are narcolepsy, obesity, mild depression states, and sometimes in acute alcoholism, for which it is a specific antidote. In combination with amytol (dexamyl) it is used to raise the pain threshold in post-operative patients.

Dosage is 10-30 mg by hypo or oral. Elimination is entirely through the kidneys, occurring only slowly, and accounting for the long duration of action.

B-Inhibitory. We now come to the newest and possibly the most interesting field of our topic, that of the sympatholytic drugs. These drugs inhibit sympathetic activity throughout the body, thus producing of clinically valuable effects. By some these are hailed as the latest "miracle drugs", and they may yet prove to be so. It must be stressed that these drugs are new, some of them so new as to be available at present only for experimental use. The scope of the field is rapidly widening, and will continue to do so as more is learned and newer related compounds developed.

The magnitude of this subject may be better appreciated when one considers the manifold functions of the sympathetic nervous system, and its importance in certain pathological conditions. It is of prime consideration in elevation of the blood pressure of the "essential" type, it is a controlling factor in synovial fluid reaction; it plays a part in such widely separated conditions as frostbite, poliomyelitis and phantom limb pain.

It must be remembered that there is an afferent as well as an efferent side to the sympathetic nervous system, and these drugs block this as well. This action is of use in many painful conditions, a few of which are dysmenorrhea,

causalgia, and pleuritis. Experiments are being carried forward at present to evaluate their use in relieving the pain of coronary thrombosis, and pulmonary infarction, and it has been established that they are of aid in relieving the pain of renal and gall bladder colic.

However, aside from their use in the relief of pain, their main field at present is in the treatment of vasospasm, ranging from hypertension to Burgers Disease.

There have been a number of drugs (ergot, yohimbine, dioxane derivatives) long known to possess anti-adrenergic properties, but these are all too toxic in therapeutic dosage for routine use. Therefore, prior to the advent of the group of drugs which follows, overactivity of the sympathetic nervous system could only be combated by stimulation of the para-sympathetic system or sympathectomy.

Dibenamine (dibenzyl beta-chloroethylamine) acts by blocking the excitatory action of epinephrine (sympathin E) and unmasking its inhibitory action (sympathin I). After therapeutic doses of dibenamine response may still be elicited by agents which act directly, such as pituitrin. Its chief use to date has been in the treatment of essential hypertension, particularly that of a malignant nature. Its use is still in the experimental stage but results have been very encouraging. It produces definite orthostatic hypotension in all subjects, and dramatically relieves the symptoms of malignant hypertension in most patients. In patients with essential hypertension the supine blood pressure level may also be adequately controlled by repeated doses. In comparison with etamon, an approximately equal drop in supine blood pressure was obtained, but a considerably longer duration of action was found with dibenamine.

Some incidental actions, which may prove to be of clinical usefulness are an increased urea clearance and increased urine volume, probably on the basis of decreased tubular resorption. Toxic reactions seem to occur in all patients, to varying degrees. They consist of nausea, restlessness and drowsiness. Dibenamine is administered by slow i.v. drip in a dosage of 2 to 10 mg. kg per day. It is possible to use oral administration in a dosage of 0.25 to 0.5 gm. one to three times daily, but the value of this method has not been evaluated.

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RESEARCH IN THE SERVICE OF MEDICINE



Etamon hydrochloride (tetraethylammonium chloride) acts by competing with acetylcholine, at the autonomic ganglia. It thus blocks parasympathetic as well as sympathetic ganglion transmission; however its main clinical effect is one of sympatholysis. It has been used extensively to relieve the vasospasm incident to Burger's Disease, and it has received limited trial in the treatment of causalgia. It may be used with benefit in any of the conditions mentioned in the introduction to the sympatholytics. It has given fairly good results in relief of the pain of gastric crises. Improvement has been obtained by its use in cases of anxiety reaction, the results sometimes being quite impressive. A field in which it may prove quite useful in the future is that of poliomyelitis, in the relief of pain and amelioration of contracture formation. The rationale of its use here is that pain in this disease is caused by ischemia, due to vasoconstriction due to overactive sympathetic outflow.

In general, this drug may be used as a substitute for para-vertebral block on a temporary basis, whenever this is indicated. Toxic effects include dryness of the mouth, postural hypotension, and occasional interference with urination and defecation. Dosage is 0.25 gm t.i.d. orally for ulcer pain. For all other conditions 3 to 5 cc intravenously or up to 15 cc intramuscularly per day. Patient should remain supine for ½ hour following injection.

Methonium compounds have actions very similar to those given above for *etamon*, but the duration of effect is longer. These are still undergoing experimental development. Dosage is 100 mg intramuscularly or 1 gm. oral t.i.d. They have the advantage of being absorbed in therapeutic concentrations from the intestinal tract.

Priscol (2-benzyl-4, 5-imidazoline hydrochloride) is an anti-adrenergic agent which has the advantage of oral administration. Its locus of action is at the end organ, where it inhibits reaction to sympathin (or epinephrine). It does not act on autonomic ganglia. It differs from other agents in this field (such as *etamon*) by causing marked increase in gastric motility, and for this reason is contraindicated in cases of peptic ulcer. The main clinical effect is that of vasodilatation, and it may be used advantageously in any condition involving vasospasm, such as Burger's and Raynaud's Diseases, peripheral vascular complications of diabetes, and

stasis ulcer. Other actions of possible clinical use include a decrease in blood sugar, both in normal and diabetic persons, particularly noticeable in elderly diabetics. Also a diuresis on intravenous injection in cases of water retention due to acute or sub-acute nephritis, and a well maintained drop in blood pressure in cases of essential hypertension.

In summary it can be stated that it is of great use as a substitute for para-vertebral block, is very useful in visceral pain due to vascular spasm, and can be given orally.

Dosage is 25 to 50 mg orally four to six times daily, or 10 to 50 mg by hypo four times daily. Side actions consist of nausea, epigastric distress or diarrhea, tachycardia, and slow rise or fall in blood pressure. These symptoms frequently disappear with continued therapy, regardless of increase in dosage.

Dibutoline—A useful antispasmodic

Leo J. Kent—*Arizona Medicine* 7:31; July 1950

Dibutoline (Dibutyl urethane of dimethyl ethyl B-hydroxy ethyl ammonium sulfate, Merck & Co. Inc) is a drug of the anti-cholinergic group which is considered here because of only recent receipt of literature. This drug is paradoxical in that it belongs to a group of chemicals (choline esters) having cholinergic properties and yet it itself has an anti-cholinergic effect. It acts by inhibiting acetylcholine at the myoneural junction, in exactly the same manner as atropine. It is claimed that it has no action on the autonomic ganglia (as does *Banthine*), and does not affect the adrenergic system. However there is a local inhibitory action on smooth muscle, which accounts for a drop in blood pressure on intravenous administration.

Its main use is in relieving cases of smooth muscle spasm of the gastro-intestinal, biliary and urinary tracts, for which purpose it has proven highly effective. It has a low toxicity, and a moderate degree of mouth dryness and pupil dilatation as side actions. Relief has been effected in cases of severe renal and biliary colic, after atropine and demerol have proven ineffective. *Dibutoline* has also been of use in cases of duodenal ulcer, pylorospasm, acute gastroenteritis, ulcerative colitis, spastic colon, and dysmenorrhea. It is very useful in post-cystoscopy spasm.

Dosage is 5 to 10 mg hypo (0.5 to 1.0 cc) repeated in thirty minutes if necessary and there-

after every three to four hours. Dibutoline is ineffective when taken orally.

This drug is not yet available for clinical use, and is still classified as a "New Drug" by the Federal Food, Drug and Cosmetic Act.

SUMMARY

A brief review of the physiology and anatomy of the autonomic nervous system has been presented, together with a description of drugs affecting it and their clinical use. The great potential field of the sympatholytics and spasmolytics has been set forth, together with some of the recent advances in this topic. It is hoped that the information presented will be of some help, and that the possibilities suggested will stimulate further clinical trial and evaluation.

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Relationship of Stress to Autonomic Lability

Studies in psychosomatics have shown that functional disorders often are a result of the patient's inability to adjust to emotionally stressful situations (stressor factors).

Nervous tension and chronic anxiety, discharged through a labile Autonomic Nervous System, can cause somatic disturbance.^{1,2} Such states may involve any one of the organ systems or several at one time.^{1,3} The outline below is designed to relate gastrointestinal and cardiovascular symptomatology to the exaggerated response of the autonomic nervous system.

	Physiologic Effects of Autonomic Discharge	
	Sympathetic	Parasympathetic
Gastro-intestinal System	Hypomotility Intestinal Atony Hyposecretion Reduced salivation	Hypermotility Gastrointestinal spasm Hypersecretion
Cardio-vascular System	Rapid heart rate Peripheral vaso-constriction	Slow heart rate Vasodilatation
Functional Manifestations	Palpitation Tachycardia Elevated blood pressure Dry mouth and throat	Heartburn Nausea-vomiting Low blood pressure Colonic spasm

The data here tabulated is from references 3,4,5,6,7, given below.

When the clinical picture is suggestive of functional disorder, the diagnosis is supported by the presence of the following indications of autonomic lability:

Variable Blood Pressure
Body Temperature Variations
Changing pulse rate
Deviations in B. M. R.
Exaggerated Cold Pressure Reflex
Oculo-Cardiac Reflex Abnormalities
Glucose Tolerance Alterations

Therapy in these cases is directed toward: 1) relieving the somatic disturbance to prepare the patient for psychotherapy*; 2) guidance in making adjustment to stressful situations and correction of unhealthy attitudes.

*Drug treatment using adrenergic and cholinergic blocking agents in conjunction with sedatives.^{8,9,10.}

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1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

Editorial

HEAD TRAUMA

Fortunately, most people who sustain head injuries recover spontaneously. In certain cases, specialized neuro-surgical measures may materially reduce both morbidity and mortality.

Emergency Care

A careful survey of vital processes and of the general physical status of the injured patient is required in order to rule out complicating in-

juries to other parts of the body. Scalp bleeding may be controlled temporarily by a pressure dressing. Unless the hemorrhage has been excessive or other injuries are present, shock is rare. Adequate pulmonary ventilation is of importance since cyanosis and hypoxia cause edema of the brain which may aggravate existing brain pathology. Cerebral injury itself may tend to induce pulmonary edema. Aspirated mucus on the tongue can superimpose a mechanical obstruction of the airway. Simple posturing is usually adequate to eliminate these factors, but an endo-tracheal tube and even tracheotomy may be indicated if adequate ventilation can be obtained in no other way. Oxygen is indicated during the period of unconsciousness.

Unconsciousness and the Lucid Interval Syndrome

An impairment of consciousness, which may vary from profound coma to a sensation of giddiness, follows brain injury resulting from head trauma. The "center" for consciousness has been localized to basal structures of the brain,—i. e., posterior hypothalamus, thalamic reticular system, peri-aqueductal gray matter. Actually, the state of consciousness and the severity of the head injury are correlated only if there is damage to this area. If the brain is recovering normally from the effects of trauma, the depth of coma should lessen in the following sequence of events:

- 1) *Coma* (no reflexes or responses to noxious stimuli),
- 2) *Stupor* (unconscious, with return of reflexes and response to pain),
- 3) *Restless confusion* (irrational, frequently violent behavior),
- 4) *Confusion* (disorientation, without restlessness),
- 5) *Automatism* (orientation, partially present but characterized by memory deficit),
- 6) *Lucid mental status*.

The so-called *lucid interval syndrome* is one characterized by a period of consciousness after a head injury, followed by a progressive loss of consciousness. This syndrome must be considered to indicate cerebral compression and constitutes a surgical emergency. Dural hemorrhage (extra-dural or sub-dural) is responsible for approximately 25% of the cases of this type. Cerebral contusion and edema, fat embolism or

pneumatocele may create this clinical picture. No explanation can be found in a few cases. The chances that a dural hemorrhage is present are enhanced if signs of focal neurologic dysfunction are present, appearing *after* the initial examination. The most reliable localizing signs are (1) ipsilateral pupillary dilatation and (2) intra-lateral hemi-paresis.

The statistical odds are somewhat against a dural hemorrhage as the cause of the lucid interval syndrome, but there is no way of eliminating the possibility without a trephination. Dural hemorrhages will cause death unless they are relieved surgically.

The diagnosis of a progressive dural or subcortical hematoma is more difficult if there is no lucid interval after the initial unconscious period. It has been demonstrated repeatedly that changes in the blood pressure, pulse rate, and respirations, frequently do not correlate with the apparent intra-cranial pressure in cases of unconsciousness after trauma. Specialized studies may be required in such instances.

Diagnostic Studies

1. *Skull x-rays* are not made until the convalescent period unless the clinical findings suggest a surgical complication, i.e., (a) scalp laceration with definite or suspected underlying fracture, (b) depressed skull fracture, or (c) lucid interval syndrome.

2. *Electro-encephalography* may be helpful in cases of the lucid interval syndrome, but is time consuming and not as direct as trephination. Its major value is in the more chronic phases to evaluate encephalopathy and epilepsy.

3. *Lumbar puncture* is of help in two particular instances:

(1) It is of limited value in diagnosis. When spinal fluid pressure is elevated in a patient with the lucid interval syndrome, the presence of a dural hemorrhage is to be strongly suspected, however, the pressure may be subnormal in some instances. Stiffness of the neck in head trauma usually indicates subarachnoid bleeding and a lumbar puncture only confirms this.

(2) The value of spinal fluid drainage in the therapy of head injuries is limited to cases of intolerable headache, nuchal stiffness and restlessness. In these patients, the initial pressure should be recorded, and fluid removed *slowly*, until the pressure has been reduced approximately 50%.

Other Therapeutic Problems

Restlessness often accompanies traumatic encephalopathy. Paraldehyde is as safe and effective as any drug in controlling this situation. Narcotics and other medullary depressants are to be avoided. The removal of a small amount of bloody cerebro-spinal fluid or the catheterization of a full bladder may relieve a restless patient, when drugs fail.

Increased intra-cranial pressure may accompany head trauma. Conservative measures to reduce edema are usually effective, including (1) adequate pulmonary oxygenation, (2) antibiotic agents to reduce the possibility of infection, and (3) normal fluid and electrolyte balance. The use of serum albumin and hypertonic solutions are being used less and less. Radical therapy consists of the removal of dural or subcortical hematomas.

Rhinorrhea and *otorrhea* indicate basal skull fractures through the cribiform area and petrous ridge, respectively. These conditions may lead to meningitis and brain abscess if the portal of entry becomes infected. Postural drainage, antibiotics and "neglect" of the affected area are usually effective prophylactic measures. The leakage from the ear nearly always stops within a few days, but occasionally rhinorrhea may persist. If rhinorrhea continues for a week or more, or if infection becomes apparent, surgical intervention is indicated.

Convalescence

Ambulation is encouraged as soon as the patient is lucid, symptom free and desires to be up. The guide to social and economic rehabilitation is good clinical judgment.

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The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

October 2, 1950

A sixty-year old unemployed carpenter was admitted to the hospital because of cough of five months' duration.

Two years before entry, the patient fell, striking his lower right chest against a stake. A roentgenogram was said to show questionable fracture of the eighth rib near the spine. After this, the patient began to have periodic pain in the region of the right nipple, occasionally radiating through to the back, to the right side of the neck and occipital region, or to the right axilla and right upper arm. These attacks occurred once or twice a week, and frequently accompanied damp weather or the lifting of heavy objects. The pain was sharp and intermittent. The patient was otherwise well and able to continue his work. Eight months before entry, there was some loss of appetite. Five months before entry, there was gradual appearance of cough productive of two or three tablespoonfuls of white sputum. The attacks of pain were aggravated by the cough. After a few weeks, the patient began to feel nauseated. Attempts at vomiting increased the cough. The sputum became foul, leading the patient to consult a physician. A roentgenogram of the chest was said to show "clouding of the right lung." The patient was given green liquid medicine and white pills. He remained in bed for about a month, with some resultant improvement in his general condition, and then returned to work. The sputum became increasingly foul and turned green. Two and a half months before entry, the sputum became pink, up to half a pint a day being raised. Gradually, the sputum became frankly bloody. Two months before entry, the patient was forced to stop work because shortness of breath. There was a weight loss of 10 or 15 pounds in the course of the illness.

The past and family histories were irrelevant. Venereal disease was denied.

On admission, examination showed a poorly nourished, chronically ill man of middle age, coughing and orthopneic. The veins over the neck and arms were prominent, more so on the left than on the right. The heart was of normal size, with a rough systolic murmur at the aortic area, poorly transmitted to the neck. Coarse rales were heard throughout the right chest, with occasional loud expiratory squeaks and groans over the right upper lung field. There was dullness over an area corresponding to the right upper lobe anteriorly, posteriorly and in the axilla. Breath sounds and vocal and tactile fremitus, however, were not altered in this area. A few small cervical lymph nodes and a solitary left supraclavicular node were palpable but not tender. The liver edge lay just below the costal margin. The abdomen was otherwise normal. There was early clubbing of the fingers. Neurologic examination was negative.

The blood pressure was 110 systolic, 55 diastolic, in the right arm and 105 systolic, 60 diastolic, in the left arm. The temperature was 99°F., the pulse 130, and the respiration 25.

Examination of the blood showed a red-cell count of 4,500,000 with 13 gm. hemoglobin, and a white-cell count of 16,000 with 84 per cent polymorphonuclears. The blood Hinton reaction was positive. The urine was normal. Culture of the sputum showed no beta-hemolytic streptococci.

A roentgenogram of the chest showed a huge irregular cavity occupying a completely consolidated right upper lobe. The cavity was about 6 cm. in diameter, and there were multiple nodular projections along its margins. There was only a small quantity of fluid. The arch of the aorta was dilated and prominent, with a suggestion of calcification. The heart was of normal size and shape. The ascending aorta was questionably prominent. There was no definite evidence of bone destruction in the ribs or vertebrae.

The patient continued to drain large amounts of foul-smelling sputum. He was given sulfadiazine. The temperature fluctuated irregularly between 98 and 105°F. On the eighth hospital day, coarse rhonchi were audible throughout both lung fields. The patient became increas-

ingly weaker, and cyanosis appeared. He was given gomenol, with good relief from the foul odor of the sputum. Death occurred later in the day, apparently from respiratory failure.

DR. LOUIS B. BALDWIN

Even by the most superficial perusal of this case one can be certain that there is a lung abscess involving the right upper lobe. The copious foul smelling sputum, gradual down hill course with fever and leukocytosis, and finally, the irrefutable x-ray evidence all point to this condition. But, to give an accurate chronological order of events leading up to the abscess is much more difficult. If one were to assume that the injury suffered two years previously was responsible for the pulmonary pathology leading to the abscess, then one would have to postulate a serious injury complicated by pneumonia and eventual suppuration. This train of events is possible, but in spite of the persistent chest pain there is no evidence of an acute antecedent pneumonia. On the other hand, Waddell, Sniffen, and Sweet describe a so-called chronic pneumonia lasting from nine weeks to ten years in which the onset may be insidious. The principal chronic symptoms were fever, cough, expectoration, and occasional hemoptysis. By x-ray a variable portion of the lung usually showed evidence of atelectasis or consolidation, and the possibility of carcinoma could seldom be excluded with certainty. Section of the affected portion of the lung showed an intense yellow color. In later stages there was a marked fibrosis. The yellow color was due to the presence of cholesterol esters. Occasionally, small abscesses were observed. If the accident had produced a chest wall injury with the development of osteomyelitis, one would expect extensive pleural involvement with empyema. Moreover, the original injury was of the lower and not the upper chest. The attractive rather simple conclusion that the lung abscess resulted from a preceding chest injury is therefore difficult to accept.

Suppurative pneumonia may be due to a variety of causes. The lungs may be involved by hematogenous implantations of septic emboli from distant foci or as a result of secondary infection following acute inflammations, such as measles and influenzal pneumonia. The most common cause is bronchiogenic aspiration of infected material from the upper air passages during operations under general anesthesia or

following trauma and unconscious states. In many instances suppurative pneumonia is synonymous to aspiration pneumonia. In other instances the disease is secondary to pathologic processes in the thoracic wall, esophagus, mediastinum, spine and other adjacent organs. Or the abscess may be secondary to other pulmonary diseases such as bronchiectasis, infarction and neoplasm. Occasionally tuberculosis may be complicated by a purulent abscess. In an analysis of 125 instances of putrid lung abscess, Sweet found that 56 per cent followed tonsillectomy or some other operation on the mouth, nose or throat; 11 per cent followed an operation on some other part of the body; a few followed normal delivery; about 4 per cent were caused by the aspiration of foreign bodies; 15 per cent followed infections of the upper respiratory tract or pneumonia. Finally in 12 per cent no cause was found.

The actual development of a putrid lung abscess, known to pathologists for many years as lung gangrene is caused by aspiration of anaerobic organisms normally present in the upper air passages of adults and found in abundance in those with pyorrhea and carious teeth. These anaerobic organisms include streptococci, fusiform bacilli, vibrios, spirochetes and grand negative bacilli acting in symbiosis.

It can be maintained from the above that the carpenter sustained a severe blow two years previously which caused unconsciousness and the production of an aspiration pneumonia, or that he might have sustained a pulmonary infarct. It is to be noted that ever since the injury there was periodic pain in the region of the right nipple radiating through to the back and to the right side of the neck. These symptoms might conceivably indicate some beginning upper right lung infection. It was not until five months before admission to the hospital that he developed symptoms of suppuration with productive cough and finally foul sputum. The x-ray at this time showed "clouding of the right lung", which is a rather vague description for our analytical purposes.

In order to cover the field of possible causes of the lung abscess other conditions must be considered.

Bronchiogenic carcinoma is not an uncommon cause of lung abscess. About 75 per cent of these tumors arise in a main bronchus. With enlargement, atelectasis develops, the tumor

penetrates the bronchus and spreads directly to the collapsed lobe. In about one third of instances Fishberg and Rubin found abscess formation. The factors leading to the development of abscess are obvious. The blocked bronchus causes a damming back of secretion which results in a suppurative broncho-pneumonia. Or else the rapidly enlarging tumor outgrows its blood supply and an anemic necrosis of the central part sets in, the necrotic tissue being eliminated through a communicating bronchus; secondary infection with pyogenic or anaerobic bacteria aids the ulceration and liquifaction. It is noteworthy that excavation occurs only in primary lung tumors according to Rubin. Three types of bronchiogenic carcinoma are recognized: (1) an epidermoid carcinoma usually of a squamous cell type; (2) an adenocarcinoma and (3) an anaplastic type, referred to as a small, spindle or round cell carcinoma.

Bronchiogenic carcinomas spread by direct extension as well as by lymphatic and blood channels. Epidermoid carcinoma, which is more common in the male, is relatively slow growing, and late metastasizing. It is not uncommon to find at autopsy instances of the latter limited to the affected lung and the regional lymph nodes without any evidence of tumor elsewhere in the body. In 3047 collected cases of carcinoma of the lung, Ochsner and DeBakey found the instances of metastasis in various organs as follows: regional lymph nodes, 72.2 per cent; liver, 33.3 per cent; pleura, 29.8 per cent; lungs, 23.3 per cent; bone, 21.3 per cent; brain, 16.5 per cent; heart and pericardium, 12.7 per cent; adrenal, 20.3 per cent; kidney, 17.5 per cent.

In 210 cases analyzed by Rubin, the present illness had existed less than a year in 60 per cent, and less than six months in 30 per cent. The history usually elicited is that of an aggravation of a pre-existing bronchitis, increasing pain in the chest, hemoptysis, and dyspnoea. There is often loss of weight over a short period of time, increasing weakness and epigastric discomfort. The vague abdominal symptoms may simulate malignancy of the gastro-intestinal tract. In Rubin's series, several of the patients traced the onset of their illness to an injury sustained some time previously, and in a few the injured site coincided with the later appearance of a metastatic deposit.

What is the evidence in this case to lead to a possible diagnosis of bronchiogenic carcinoma?

In the first place there is the age of the patient which is in the common cancer period. Then there are the enlarged cervical lymph nodes with a "solitary left supraclavicular node." Again, the slightly enlarged liver might be due to hepatic metastasis, and finally there are the prominent veins over the neck and arms, more so on the left than on the right. This might indicate metastasis around the subclavian vein with vascular obstruction. To be sure there is no anemia but there may be a compensatory polycythemia in keeping with the pulmonary osteo-arthritis to mask this condition. Unfortunately, in the differential diagnosis between putrid lung abscess and broken down carcinoma, the roentgenogram is of little help, because in each instance there may be scalloping in the wall of the abscess, though this finding is more common in the carcinomatous abscess. The "multiple nodular" projections noted in the present case may therefore be due to a non-malignant abscess.

In a differential diagnosis of the cause of lung abscess, pulmonary cyst must be considered. There may occasionally be solitary and may become infected with the production of a lung abscess. There is nothing in our case to indicate a pre-existing cyst of the lung.

Tumors of the mediastinum must also be considered. A dermoid cyst of the anterior mediastinum might conceivably invade the lung with the development of a secondary lung abscess. The same could be said about the neurogenic tumors of the posterior mediastinum, although in each instance careful x-ray studies should reveal the mediastinal nature of the tumor.

Among other rare causes of lung abscess may be mentioned blastomycosis and actinomycosis. In these fungus infections there is more apt to be wide spread pulmonary involvement. I can see no evidence in this case of infection due to a fungus. Amoebic abscess of the lung and hydatid cyst almost invariably involve the base of the lung and not the apex.

From this survey of the possible causes of lung abscess the final diagnosis seems to rest between suppuration due to an antecedent injury or infection of the lung and bronchiogenic carcinoma. If the former proves to be the case there might well be a mediastinal or bone infection extending to the lung. One would have to postulate a low grade suppuration initiated at the time or shortly after the injury of two

years previously, eventually spreading to involve the lung. It is inconceivable, under such circumstances, that the morphology leading to the abscess had existed in the lung for a matter of two years without more striking evidence of chronic disease. Taking everything into consideration the diagnosis of bronchiogenic carcinoma is more probable. The positive Hinton is of no significance in the etiology of the abscess, even though in the older literature gummata of the lung were described, similar clinically to caseous or fibro-caseous tuberculosis. Excavation has been described with the development of an abscess. The changes due to syphilis are said to be more common in the deeper parts of the lung near the roots and the lower lobes. In view of the calcification in the dilated arch of the aorta seen in the x-ray, arteriosclerosis of the aorta seems more likely than aneurysm due to syphilis.

1. My first choice of diagnosis is bronchiogenic carcinoma, epidermoid in character with the secondary development of putrid lung abscess and metastases to lymph nodes.

2. My second choice would be chronic lung abscess.

DR. BEN P. FRISSELL

We have today a problem of differential diagnosis of gangrene or putrid abscess of the lung. It will be conceded by all, I believe, that this man died of sepsis localized in the upper right lung field. The origin of this process requires consideration.

We are given a 60-year old carpenter who dies on his 8th hospital day who apparently presents himself for hospitalization five months after he began to complain of cough productive of small amounts of colorless sputum which gradually changed character from mucoid and odorless to purulent and foul and, subsequently, to pink and frankly bloody purulent sputum.

There is no history given to indicate fever at the onset of this illness and no evidence of chest pain at the onset. Three months before the patient first noticed cough, he noticed lack of appetite. Along with the symptoms of cough, he developed nausea. His cough was aggravated by vomiting. During the period of several months before his admission to the hospital, he lost 10 to 15 pounds in weight and entered the hospital in a poorly nourished or emaciated state.

Two years before admission, the patient suffered an injury to his right chest, presumably falling against a stake while at work as a carpenter, striking his lower right chest. X-ray was said to show questionable fracture of the eighth rib posteriorly. Presumably, there were no other pulmonary findings on x-ray at that time. Following this injury, the patient began to complain of periodic pain in the right chest anteriorly. He also had pain radiating to the right side of the neck, the occipital area, and the right axilla and upper arm. These attacks were periodic and were aggravated by damp weather, lifting, etc. The pain was sharp and intermittent. The patient continued to work, however. He felt well otherwise for a year and a half after his injury.

On examination, at the time of hospital admission, there were evidences of extensive involvement of the entire right upper lobe apparently, with dullness and coarse rales throughout this area. There were no definite physical signs of cavitation but an x-ray revealed a large irregular cavity occupying a completely consolidated right upper lobe. The cavity was described as about 6 cm. in diameter with multiple nodular projections along its margins. It contained a small amount of fluid. The arch of the aorta was dilated and prominent with suggestive calcification compatible with the age of the patient. There was no evidence of bone destruction, no mention of any mediastinal shift. At the time of admission to the hospital, the patient was raising about $\frac{1}{2}$ pint of purulent, foul-smelling, bloody sputum. There were noted on examination small cervical nodes (we are not told whether they were left or right, or both) and a solitary left supraclavicular node. The neck veins were described as full, particularly on the left side. We note these findings in spite of the fact that the lung findings were limited to the right chest. There was no notable variation in the blood pressure reading of the right and left upper extremity. The patient was coughing and having definite respiratory difficulty. There was increase in pulse rate and respiration.

Given then a putrid abscess or gangrene of the right upper lobe in an elderly man with a history of injury to the right chest two years before his death, what are the diagnostic possibilities: Lung abscesses have been variously classified and are due to a multitude of causes.

Judd offers a simplified classification which would appear adequate for our needs in this discussion: (1) Inhalation or aspiration-type abscesses. Seventy per cent of lung abscesses are said to follow post-tonsillectomies or dental extractions and an additional 12% are said to follow other post-operative procedures where a general anesthesia is used, thus accounting for better than 80% of suppurative lung lesions. (2) Respiratory-type abscesses following either infections of the lungs, such as acute pneumonia or chronic lesions such as bronchiectasis and obstructions to the bronchial tree from various origins including malignancy, of course. This group accounts for 15% of such lesions. (3) Embolic abscesses arising from septic infarcts, etc. This latter group and the small percentage of lung abscesses of undiagnosed or unknown origin account for the remaining 5% of lung abscesses, according to Judd's classification.

I believe that we can dispense with the first group from the history alone in the case at hand. We have no knowledge of foreign body aspiration or of surgery of any type. The third group raises the question of a septic embolus which of course brings up any possible connection with the original injury one and a half years before the onset of the patient's symptoms referable to his lungs. The onset, in the first place, is not that of an infarct. We have no history of pain and bloody sputum and an embolus or infarct, unless massive, would be expected to be peripheral in its location whereas this lesion apparently originated in the hilar region of the lung. Dr. Moore could probably elaborate for the rest of the afternoon on the industrial implications of this case, assuming that this man's original injury was of that nature and, if it occurred in Arizona, undoubtedly it would have been. We are all well aware of the tendency of patients, particularly industrial, to tie in the symptoms with traumatic experiences however remote and unrelated they might appear from a medical standpoint.

This brings us down to the second group of the so-called respiratory abscesses. First, let us consider the infections, or rather the non-obstructive respiratory lesions which might enter into this situation. I would like to dispose at this point of one red herring; i.e., the positive Hinton. We have all been educated in our earlier years as to the diagnosis of syphilis of the lungs and we have heard that diagnosis made and

discussed in this Clinic but, to my knowledge, never authenticated. And I choose today to go along with this school of thought which holds that this entity, although much talked-of and discussed, seldom, if ever, is seen.

Tuberculosis: Does not appear to be worthy of much comment, although Dr. Williams has given us a very brief, concise analysis of the sputum, leaving this possibility open for us to think about. The age of the patient, appearance of the cavity and the lung field by x-ray are against this diagnosis.

Cystic disease of the lung: Not likely. Negative x-ray two years before death, an elderly man, solitary abscess. I am thinking of course of the so-called congenital cystic disease. Hydatid cyst of the lung, likewise not likely. This type cyst is usually in the lower right lung field in the areas adjacent to the liver, from which this lesion reaches the lung usually by direct extension.

So-called fungus infections of the lung, notably coccidioidomycosis and actinomycosis may be mentioned. Sputum studies, appearance of the lung on examination are certainly not characteristic or suggestive of coccidioidal infection, and, on this basis alone, I would rule out this diagnosis. Actinomycosis, I do not feel is likely. We have no history of exposure. The onset is not typical, there are no draining sinuses which are common in this disease, the character of the sputum is not described for this syndrome. The diagnosis, of course, is made by sputum analysis.

In considering the pyogenic lung abscess, we are undoubtedly dealing with the so-called putrid type of abscess which signifies anaerobic bacterial flora; i.e., anaerobic streptococcus, Vincent's organisms, etc. The onset of symptoms is not characteristic of the post-pneumonic or influenzal-type abscess nor do we have a history compatible with a diagnosis of long-standing bronchitis, or bronchiectasis which, in the typical instance, would be involving the lower lung fields, probably bilaterally.

This leaves us with the group of so-called obstructive lesions capable of producing atelectasis and subsequent infection and abscess formation to the point of pulmonary gangrene. Neoplasms enter into this situation quite prominently. From the sequence of events in this case, it is my conclusion that we have had for an indefinite period of time, probably up to two

years, a progressive obstructive lesion with involvement of the right upper main stem bronchus and other mediastinal tissues, particularly in the upper mediastinum. There is a good possibility that there has been involvement of the apical portion of the lung as evidenced by symptoms of pain in the right shoulder, pain down the right arm, and pain up the right side of the neck indicating the possibility of some involvement of the brachial plexus, which is not an uncommon symptom in one type of carcinoma of the lung, the so-called apical carcinoma spreading along the lymphatics and the pleural surfaces. This type of cancer usually invades locally, seldom metastasizes, although it may erode the bony rib cage in some cases. Compression symptoms are quite common. This type of tumor would undoubtedly explain a good portion, if not all, of the patient's post-traumatic symptoms of pain over a period of two years because the invading process may involve the upper mediastinal structures and the superior pleural surface of the lung a relatively long time before obstructive symptoms occur from involvement of the main stem bronchus. Tumor growths capable of producing this picture can either originate in the lung, they may be benign or malignant, or may be metastatic from other malignant sources in the body with metastases to the mediastinal glands and subsequent obstructive symptoms. They may be primarily lymphatic in origin in the mediastinal structures, notably the so-called malignant lymphomas including in this classification Hodgkin's disease and lymphosarcoma, particularly.

To differentiate these groups is beyond the scope of this discussion because the final diagnosis will have to lie on bronchoscopic findings, and, or, microscopic studies as the result of surgery, or autopsy. Numerous so-called benign lung tumors have been described. Most likely if we were dealing with this diagnosis in this case it would be the so-called design bronchial adenoma which some investigators feel may be a precursor to definite adenocarcinoma in late stages of the disease. The indications of some gastrointestinal tract involvement in the early stages of this man's symptomatology raises the question of a metastatic lesion arising in the stomach. The palpable left supraclavicular node has often been described as a sign of stomach carcinoma. Any time this lesion is found, deeper-seated mediastinal gland involvement must be

anticipated. Likewise, the findings of compression involving the left mediastinum suggest primary mediastinal involvement. However, simply because we have definite involvement of the main upper right stem bronchus is no reason to conclude that the lesion could not be also involving other mediastinal structures through lymphatic spread. Among the symptoms of carcinoma of the lung is frequently mentioned the incidence of anorexia and vague dyspeptic and upper gastrointestinal symptomatology. This is not too mysterious when one considers the close proximity of the esophagus to the main stem bronchus, the carina, and the adjacent mediastinal structures.

I am inclined to go along with Rubin, Judd, and other investigators who feel that in obscure lung lesions occurring in elderly individuals, a diagnosis of cancer of the lung is present until definitely proved otherwise. We are all aware of the apparent increasing incidence of pulmonary carcinoma. A disease which a few decades ago was considered a rarity is now known to be quite common. A recent survey of the autopsy reports from Montefiore Hospital in New York City, show carcinoma of the lungs occurring in 5% of their autopsies during the period from 1914 to 1944. Other hospital reports indicate 1% to 2% incidence of lung carcinoma and 10% of all carcinoma cases. A 1942 census report indicated approximately 6,000 deaths from this disease. Several factors are concerned in apparent increase in incidence of this disease: (1) An aging population, (2) Improved methods of diagnosis, particularly bronchoscopic surveys, and biopsies, laboratory smear technique, etc. (3) Recent work on inhalation irritants including tobacco smoke. The age incidence of carcinoma of the lung is 40 to 60. Males outrank females three to one. The origin is usually in a major bronchus in 75% of cases. Periphery of the lung is involved in only 25%. The upper lung field is involved in most instances. Complications include atelectasis, emphysema, and abscess formations in about 35% of cases, particularly when there is involvement of the main stem bronchus. These changes originate from impaired circulation, obstruction, and secondary infection. Metastatic lung tumors in the peripheral or mid-lung fields rarely suppurate but this does not hold for the metastatic involvement of the mediastinal structures producing secondary involvement of the bronchus.

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Histologically, carcinoma of the lung can be divided into three main types: the so-called epidermoid or squamous cell type originating from the outer layers of the bronchial mucosa most likely to produce obstructive symptoms, in my estimation, most likely to have been the cause of this man's death; adenocarcinoma arising from the submucous layer of the bronchus; and the so-called anaplastic or spindle-cell type originating from the deeper structure of the bronchial mucosa. The last type is less differentiated and, has a tendency to more widespread metastases than the first two types mentioned. The symptoms of carcinoma of the lung are quite variable. The onset is usually insidious. The duration of symptoms before diagnosis: 30%, six months; 90%, one year. The duration of symptoms before death usually two years or less. Certainly all of the symptoms that this man presents could be explained on the basis of the above diagnosis. To mention a few: Cough, tendency to recurrent pulmonary infection, pain in the chest, hemoptysis, dyspnea oftentimes out of proportion to x-ray findings, noisy respirations, loss of weight (this is invariable), increasing weakness, epigastric distress, minor gastrointestinal symptoms, cachexia, history of injury is obtained in a great many cases that have been studied, clubbing of fingers may occur in the late stages of the disease. Review of our protocol would reveal that most, if not all, of these symptoms, are exhibited in our case. Symptoms of infection and development of abscess of a fetid type are not uncommon, abscess formation and empyema occurring in the terminal stages of a good percentage of cases.

IN CONCLUSION, I believe that our patient died of gangrene of the lung specifically the right upper lobe on an obstructive basis most likely due to primary bronchogenic carcinoma, so-called cancer of the lung, or conceivably due to metastatic carcinoma from the upper gastrointestinal tract or malignant lymphoma of the mediastinal structures.

DR. JAMES R. MOORE

This was a chronically ill, poorly nourished man—I'll not say, as might some of my younger colleagues, "old man"—of 60 years. He had been in apparent good health until eight months prior to his death, aside from periodic chest pains which followed a fall and contusion of the right lower chest two years before. This

injury, incidentally, is discounted as having no significant connection with his final illness.

He had a prominent, dilated mildly calcified aortic arch, an aortic systolic murmur, prominent veins of the upper extremities, and a positive blood Hinton. If this were all, we would say he had an aortic aneurysm, and he probably did, but more significant findings as related to his acute illness are present in the lungs. The entire upper lobe of the right lung was completely consolidated, in which there was a six centimeter cavity showing nodular marked marginal projections. There was only a slight amount of fluid present in the cavity. A productive cough had appeared five months before entry into the hospital. At first there were only two or three tablespoonfuls of a white sputum daily but it gradually increased in amount becoming green and foul, and within two months as much as a half-a-pint daily was raised. When the sputum became profuse it was tinged with pink, and later became frankly bloody. The record is strangely silent with reference to examinations of this sputum except to state that a culture of the sputum showed no beta-hemolytic streptococci.

Blood examination showed the R.B.C. and hemoglobin components to be holding up remarkably well. There was a moderate polymorphonuclear leucocytosis of 16,000 which would be consistent with the demonstrable lung infection and septic fever accompanying it. The above lung findings of:

1. X-ray evidence of consolidation with cavity formation.
2. Cough with quantities of foul bloody sputum, and
3. A septic fever, certainly mean lung abscess.

This however, does not constitute a complete diagnosis as the causes of the lung abscess are many and varied.

1. Foreign body can be reasonably ruled out in this case from the negative history.
2. Bronchiectasis; there was no previous history of this condition and the location of the principle pathology as shown by X-ray would be against bronchiectasis.
3. Abscess formation in the so called "unresolved pneumonia"; again there is no history of such infection in this case.
4. Abscess formation following infarction of the lung from a pulmonary embolus; again there is no such history present.

Refresh...add zest to the hour



5. Secondary infection and abscess formation in a tubercular consolidation.

6. The development of a secondary infection and abscess in an area of atelectasis, secondary to bronchial blockage.

The most common, as well as the most important cause of bronchial blockage, is bronchogenic carcinoma. From a consideration of the onset, progress, physical and laboratory findings, I think this man had a bronchogenic carcinoma, involving branch of the upper main stem bronchus on the right, with occlusion and resulting atelectasis of the upper lobe, an abscess that developed in this area as a result of secondary infection, with death occurring from the toxic state.

From recent literature the following brief, rather dogmatic, statements with reference to cancer of the lung have been gleaned.

1. Bronchogenic carcinoma may simulate any pulmonary disease, but none more successfully than tuberculosis.

2. The X-ray appearance may resemble (a) benign tumors, (b) tuberculosis (c) filled cysts (d) chronic abscess (e) localized bronchiectasis.

3. The symptoms, physical signs and clinical

course are not characteristic, and do not assist in the diagnosis of early bronchogenic carcinoma.

4. The only hope for a cure is by surgery in the stage before the above symptoms, physical findings and clinical course, become suggestive of the condition.

5. Diagnosis of early bronchogenic carcinoma depends upon the presumptive x-ray findings.

6. It is wise to consider abnormal lung shadows in men over 40 years of age as caused by cancer until proven otherwise.

7. Exploratory thoracotomy when in doubt is the safest course. Palliative treatment, rest cures, and watchful waiting result in deceptive responses and greatly lower the chances of successful treatment.

8. Mass surveys, even by miniature x-rays, will increase the incidence of early detection and enhance the chances for successful treatment.

In reference to the case under discussion it is suggested that bronchoscopy may not have been done because of the advanced stage of the disease when he was first brought to the hospital. No record is contained in the file with

reference to cellular study for tumor elements, but this may have been before the advent of the Papanacalou stains. The fact that the record of treatment contains no mention of anti-biotics may date this case as having occurred before the age of the "miracle drugs," and cytological diagnosis.

SUMMARY:

In summary then, my diagnosis is as follows:

1. Lung abscess in atelectatic lobe, secondary to bronchial blockage, by carcinoma.
2. Possible luetic aortitis and early aneurysm of the aortic arch.

DIFFERENTIAL DIAGNOSIS

Dr. Edward D. Churchill: We know that breath sounds are widely transmitted throughout the chest. I examined a man yesterday whose entire right lung had been removed three years previously: in the right axilla, there were normal breath sounds, tactile fremitus and vocal resonance. He had a thoracoplasty, but the transmission of the sounds from the left lung suggested a normal right lung in the axillary region. Pulmonary resection is giving us a new concept about transmission of sounds into the area over which one is listening with a stethoscope. The x-ray film in the case under discussion makes it obvious that the underlying lung could not produce normal breath sounds. They must have been coming through from adjacent segments of lung.

"There was early clubbing of the fingers." I do not like the term "early". It implies that in a few months it will increase. We have no evidence for that. Some diseases give slight clubbing, others extreme clubbing, and others no clubbing of the fingers. The term "early" means slight or moderate.

I often wish we had a more ample terminology to describe the odor of the sputum because so often the diagnosis can be made by this means alone. Varying odors of the sputum are like the bouquets of vintage wines. The word "foul" does not mean anything and, in addition, always startles the patient. It may be more informative to ask if the sputum has a bad taste. The patient will tell you that his sputum tastes bad, but if you ask if it is "fowl," he will say no. It is unfortunate that we are lacking a precise descriptive vocabulary for the subtle odors so useful in clinical medicine.

The x-ray film is quite important. There is a huge irregular cavity within a homogeneously

dense right upper lobe. The x-ray department are overstepping when they refer to a "consolidated" right upper lobe if they imply consolidation in the pathologic sense. The cavity is 6 cm. in diameter. There are multiple nodular projections along its margins.

Will you comment on the x-ray film, Dr. Schatzki? Do you care to make a more clearly definitive statement regarding calcification and prominent of the ascending aorta?

Dr. Richard Schatzki: There is definite calcification in the arch of the aorta. I should say that the ascending aorta is dilated, and also the arch. The descending is normal in size so far as I can see on the film.

Dr. Churchill: Is the heart of normal size?

Dr. Schatzki: Yes.

Dr. Churchill: Is there anything to add to the description of the cavity?

Dr. Schatzki: I think it is a fairly good description. You are right in considering the term "consolidation" a poor one. It is very often erroneously used in the sense of density, as you know.

Dr. Churchill: Let us take up the question of cardiovascular disease. There was a positive blood Hinton reaction, a dilated aorta, with calcification in its walls, a rough systolic murmur over the aortic area and a blood pressure of 110 systolic, 55 diastolic.

Dr. Breed, do you want to pick that up from the medical standpoint and tell us what was wrong with the cardiovascular system?

Dr. William B. Breed: I do not believe that the variation of blood pressure between the right and left arms was more than normal. The mere recording of such figures tends to call more attention to the variation than is justified. The pulse pressure of 50 to 55 without an aortic diastolic murmur is not particularly significant, and in the x-ray picture the possibility of syphilitic aortitis is not so likely as an arteriosclerotic aorta in a man of sixty. However, I should like to question Dr. Schatzki a little more specifically on that point—can one differentiate by this x-ray film a syphilitic from an arteriosclerotic process?

Dr. Schatzki: You mean so far as tortuosity and dilatation of the aorta are concerned. In a large number of cases of syphilitic aortitis, we call the aorta normal, knowing that we cannot see significant pathologic changes in many of them. We usually make an understatement

rather than an overstatement in that respect—it is better not to call the aorta dilated than the other way around. But when we say dilatation, I think it is quite dilated, and this particular aorta was dilated in that sense. There is not such a degree of dilatation in arteriosclerosis unless there is a dissecting arteriosclerotic aneurysm.

Dr. Breed: You never speak of a tortuous aorta as dilated?

Dr. Schatzki: We should not per se. I think that is a definite mistake.

Dr. Churchill: Do you say that this was syphilitic aortitis?

Dr. Tracy B. Mallory: How about the calcification?

Dr. Schatzki: I should say that syphilitic aortitis with dilatation shows calcification in a very large percentage of cases. As a matter of fact, the presence of calcification rather proves than disproves the diagnosis, particularly if the calcification is in the ascending aorta.

Dr. Churchill: Do you agree with that Dr. Mallory?

Dr. Mallory: I agree with Dr. Schatzki that calcification in the thoracic aorta is unusual in the arteriosclerotic aorta except in advanced cases; in the abdominal aorta, it is a different proposition.

Dr. Schatzki: I cannot see calcification in the ascending aorta. We often see calcification in the arch of an arteriosclerotic aorta, just where we see it in this particular case. If it were in the ascending aorta, it would be more in favor of syphilis.

Dr. Mallory: I should have qualified my statement. Calcification is common in the arch. A favorite spot is the dimple of the ductus arteriosus. In the ascending and frankly descending portions, I do not believe we often see it.

Dr. Schatzki: We do in very advanced cases.

Dr. Churchill: Dr. Breed, you are still my medical consultant. What do you call this?

Dr. Schatzki: If the patient had no definite evidence of regurgitation, I do not see how we can decide the question. Is that right?

Dr. Breed: Yes, he had no diastolic murmur. This does not rule out syphilitic aortitis, but it is evidence against it.

Dr. Schatzki: The fact that the heart shadow was normal probably rules out aortic regurgitation.

Dr. Breed: Yes, probably.

Dr. Fuller Albright: Was the aortic second sound recorded?

Dr. Mallory: There is no note on that.

Dr. Churchill: Then you interpret this, Dr. Breed, as syphilitic aortitis?

Dr. Breed: I shall take the arteriosclerotic side, for the sake of argument.

Dr. Schatzki: I shall take the syphilitic side.

Dr. Churchill: We know that the patient had a pulmonary abscess, with a fluid level in a cavity and foul sputum. The only question is, was this abscess in the center of a cancer, or was it not? We have no direct evidence for cancer other than the x-ray film and the course of the patient, which, however, is perfectly consistent with a noncancerous lung abscess. The history and physical examination do not point either way. The question whether or not this was an abscess within a cancer comes down solely, it seems to me, to interpretation of the film. I maintain that the thickened wall, with the nodule extending into the cavity, indicates that it was a necrotic tumor—a primary cancer. I can come to no other diagnosis. That is an x-ray diagnosis, and I should like to check it with Dr. Schatzki.

Dr. Schatzki: You must remember the cases in which we used the same reasoning and were wrong! In those cases, a markedly irregular outline of the inside of the cavity turned out to be caused by debris in an abscess.

Dr. Churchill: I do. The debris abscess gives a thumbnail appearance, rather than the picture presented by this case.

Dr. Schatzki: I agree; and from this film I should not hesitate to call it cancer.

Dr. Churchill: I can reach no other conclusion on the evidence. The clinical course could go with either. So that, purely on the x-ray visualization of the lesion, I say lung abscess within a primary cancer of the lung.

Dr. Mallory: Do you accept Dr. Breed's or Dr. Schatzki's opinion regarding the aorta?

Dr. Churchill: I have no competence to decide between them. I shall let the two gentlemen argue it out.

Dr. Breed: Dr. Albright suggests that if this was cancer in the right upper lobe, it may have pushed the aorta over to make it appear larger than it was. I think that is a good point.

Dr. Schatzki: I think we can differentiate between tortuous aorta and dilated aorta if it is markedly dilated.

Dr. Mallory: Would anyone care to defend a primary aneurysm occluding a bronchus by external pressure and secondary abscess of the lung?

Dr. Churchill: I am not willing to accept this as aneurysmal phthisis.

Dr. Oliver Cope: Would Dr. Churchill mention gumma with abscess?

Dr. Churchill: I can mention it.

Dr. Cope: And would you exclude it?

Dr. Churchill: Not definitely. I can mention it as one of the things that turn up now and then when we are wrong. It is like the safeguard of the medical student who always puts syphilis down at the end of a list to include everything in his differential diagnosis; it might be syphilis.

CLINICAL DIAGNOSES

Carcinoma of lung, with secondary abscess.
Syphilitic aortic aneurysm.

DR. CHURCHILL'S DIAGNOSES

Carcinoma of lung, with secondary abscess.
Cardiovascular disease involving aorta, nature undetermined by medical and radiologic consultants.

ANATOMICAL DIAGNOSES

Carcinoma of upper-lobe bronchus of right lung, with secondary abscess.
Metastasis to regional lymph nodes and left adrenal gland.

Syphilitic aortitis with aneurysm.

Bronchopneumonia, terminal.

Urolithiasis medicamentosa (sulfadiazine).

PATHOLOGICAL DISCUSSION

Dr. Mallory: Autopsy showed a mediastinum filled with a large aneurysm, syphilitic in origin. It replaced the arch, half the ascending the almost two thirds of the descending aorta, stopping sharply at a point about 4 cm. above the diaphragm. The dilated descending aorta has been reflected over the left lung. The cavity in the right upper lobe appears black, and a white tumor nodule is visible in the bronchus to the upper lobe. Smaller tumor masses surround the cavity. The syphilitic aneurysm was apparently coincidental and had nothing to do with the symptoms.

Dr. Breed: Then it is merely an academic discussion of x-ray diagnosis. The disease had nothing whatever to do with the patient's health or death.

Dr. Mallory: So far as this cardiovascular syphilis is concerned?

Dr. Breed: Yes.

Dr. Mallory: That is true.

There were metastases to the adrenal glands. They were the only distant metastases found.

Dr. Churchill: Was it an epidermoid carcinoma?

Dr. Mallory: It was so undifferentiated that we did not classify it.

Dr. Schatzki: Where did the dilatation start?

Dr. Mallory: It began shortly above the valve, 1.5 cm. to be exact, but was only slight, measuring 8 cm. in circumference up to the arch; then it widened to 10 and 14 cm. farther on.



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TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER, M.D.

The newest announcement of help for ARTHRITIS is that of Milwaukee's Tufts, Pessin, and Greenwald. . . . They have obtained a serum from placenta and umbilical cords which they call P.B.S. (PLACENTA BLOOD SERUM). . . . Nine patients have been treated with success; all maintained the gain after cessation of the therapy; and none have had acute corticoid effects. . . . This fits in with the remissions during pregnancy which Hench has stressed, but its value (like that of transfusions from pregnant women) remains to be confirmed.

Dr. Edgar Gordon, onetime contributor to this journal, has done it again, herewith. He is reported, in HOSPITAL MANAGEMENT, as having given a paper at the Armour Laboratories' Second Clinical Conference on ACTH. The INTRAVENOUS 'CONSTANT DRIP' USE OF ACTH produces a long "stimulation pressure" on the adrenals, and the total effect is said to be about 20 times that of a single subcutaneous injection. . . . Iso-

lated case-reports of the successful use of ACTH in black-widow spider and snake toxicity were given by other authors, and are being checked by further study in humans and animals.

It is estimated that A PATIENT PAST 65 YEARS OF AGE has 55 in 100 chances of dying from cardiovascular disease. . . . Neoplastic causes can be specially considered at earlier ages if the family history is suggestive. A predominance of carcinomas and an absence of C.-V. lesions in several generations of a family might allow one to not only be alert for neoplasms, but even point the site where they are most likely to occur.

The FAMILIAL TENDENCY OF CERTAIN CARCINOMAS has been mentioned in this column. An article on multiple neoplasms was published in ARIZONA MEDICINE about two years ago. . . . Vanden Berg of Grand Rapids, Michigan, has recently reported an amazing family in which the mother, two daughters, and a granddaughter

have had breast tumors. In addition, the mother and daughters had bilateral tumors. Furthermore, the sequence of development in each was the same—left breast, right breast. To be more coincidental, the lesions of the daughters were identical in each breast—2 o'clock, 3 o'clock. And finally, the granddaughter has her first tumor at the age of 36 years in the LEFT breast, and at 2 o'clock.

The Schering Corporation's ABSTRACTS OF MEDICAL ARTICLES IN LAY JOURNALS continue to be interesting. . . . Some of the subjects one could predict, such as "Are You A Fertile Male" from *ESQUIRE*, "The Look You Like Is Yours For The Eating" from *SEVENTEEN*, and "Why Can't Our Mothers Breast-Feed?" from *The Ladies Home Journal*. . . . Other titles are hardly predictable, tho. The *SAT. EVE. POST* comes up with an article on stellate ganglion blocks for apoplexy; *PAGEANT* has one called "Good News About Miscarriages"; and *CORONET* tops the list with "Does Rhythm Work In Birth Control?"

A few unfortunate physicians do not have access to *ARIZONA MEDICINE*, but may be able to read *GOOD HOUSEKEEPING*. For those who can read *A.M.* but not *G.H.*, we can report the medical aspects of the latter journal. . . . As has previously been said, women are served their medical knowledge in strong doses. A monthly page called 'Keep Up With MEDICINE' is composed of about ten paragraphs on such topics as the modern therapy of Parkinsonism, the electrophrenic respirator, the four chief regulators of vital processes (enzymes, hormones, vitamins, and genes), etc. . . . In the January issue there is also a 14-page section called the 'Comprehensive Home Medical Chart', prepared under the supervision of Dr. Morris Fishbein. One portion provides definitions of medical specialists; another catalogues the diagnosis and treatment of skin disorders; a third does the same thing for 'winter ailments'; a fourth shows the use of preventive inoculations; and a final two pages gives the indications for 16 standard tests and their significance. . . . Very graphic and useful, with quite a few points of interest to physicians—or can you recite quickly the interpretation of the Schick and Dick tests?

Herrell of the Mayo Clinic has confirmed other work on the wide 'spectrum' of action which aureomycin has in *PNEUMONIAS*. . . . Since it is effective for infections caused by many bacteria and viruses, it may even be 'given for pneumonia, period!' when bacterial studies cannot be made. . . . This brings us back to the suggestion attributed to a Harvard student in 1943,—“Admit the patient to the hospital. Give penicillin for 24 hours. If there are still complaints at that time, take a history and do a physical.”

The journal 'Minnesota Medicine' has several recent papers on various aspects of THE LUNGS. . . . Dr. Eugene Pendergrass of Philadelphia gives a solid but modern summary of The Roentgen Diagnosis of Silicosis. He includes an analysis of the piezoelectric theory, a conception of Evans and Kascht which was reported in this column before its publication (thru the courtesy of Dr. Oscar Sander). . . . Dr. William Eisenstadt of Minneapolis describes The Management of Status Asthmaticus better than Barach and others have done, and as tho he had learned it in Arizona. Actually, he quotes the late Dr. Kibler of Tucson, and his summary of methods is well worth while. . . . The third paper is an intriguing discussion of Ciliary Action and Atelectasis by Dr. A. C. Hilding of Duluth. The physics and Physiology of the bronchi are contrasted with those of the sinuses, the ear, and the anterior chamber of the eye, of all places.

The combination of an anti-histamine agent with 'cold' tablets was bound to come, and has. . . . Some peculiar restraint has prevented the addition of vitamins and antibiotics, but such a move might have made the pills more useful. . . . The current preparation is very nearly based on the formula $O+O=O$, according to the general feeling about oral 'cold' vaccines, and even the anti-histamines.

BROMINE INTOXICATION has been re-emphasized by Perkins of Boston City Hospital in the Archives of Internal Medicine. . . . He reported a number of proved cases, and stated that 5 per cent of cases admitted to a mental hospital have brominism. M.D.'s are responsible for about 50 per cent of the cases. . . . The signs are difficult, multiple, and variable, but the spinal fluid protein is elevated in two-thirds of those intoxicated. (An 'Arizona Medical Problem' in the March 1949 *ARIZONA MEDICINE* was a fine example of the confusion which bromides can produce in patient and his diagnosis.)

It would seem that Phoenix and Tucson might be ideal locations for a SOCIAL SERVICE CONSULTANT, employed by the medical societies themselves. This idea is a part of the famed Alameda County plan, but can be used by itself when the profession wants or needs to estimate the financial status of transient or recently arrived families. . . . The right person could be invaluable as an investigator and counsellor, and a 'fair-fee setter' in such cases.

The people from Boston are often ridiculed, and sometimes considered to be decadent. This may be done gently, as by Cleveland Amory (once of Tucson, and always of Boston) in 'The Proper Bostonians', or in several books by J. P. Marquand. . . . One may also rib fair Harvard in many ways, but rarely about medicine and never about

hematology. In recent times they have had several of the most notable hematologists in the world. Dr. Minot has just died. Dr. Castle described the theory of pernicious anemia. Drs. Strass, Taylor, Heath, and others, have formed the nucleus of the noted Thorndike Laboratory, along with the other two. Dr. Diamond has been Chief of the National Blood Bank consultants, as well as a pioneer in erythroblastosis. A handy transfusion method was recently described by a Bostonian. . . . Now Dr. Edwin J. Cohn has developed a new machine which speeds the continuous processing of whole blood into 9 fractions in a period of hours instead of several days. The fractions may be kept for a year instead of a month. . . . A 32-foot trailer truck has been constructed which is actually a blood refinery on wheels. It can handle 200 pints of blood per day, and glean the crop from a wide area.

Drs. Bacon and Sherman have listed the factors which have reduced the mortality rate following RESECTION OF THE COLON from 20% to 5% in the past 10 years. . . . A good preoperative protein balance, including a high intake of protein concentrates; intestinal antiseptics, with oral sulfathalidine for days and oral streptomycin for 2 days pre-op.; penicillin IM after surgery; oxygen saturation during the immediate post-op. period, using the BLB mask when sedation is greatest; 2,500 to 4,000 cc. of fluids parenterally until that amount can be taken orally (5% glucose preferred to saline; whole blood used as indicated by R.B.C. count and hematocrit); Wangenstein suction and Babcock sump drain for 2 to 3 days, until peristalsis begins; close observation for phlebothrombosis and thrombophlebitis, with I-V heparin and oral dicumarol if indicated; early ambulation, with patients up on the first or second post-op. day. . . . These methods allow operation on the older age groups, with little greater hazard.

One of the more ghoulish ways to sell a book has recently been presented to physicians. The book is a 'satire' (sic) on morticians. . . . Physicians are urged to buy it by the author on the tenuous and unrelated grounds that HIS father was a doctor. . . . The names of the book and author are deliberately not mentioned here on the grounds that G. Osler's father was also a doctor.

"One teaspoonful of salt, one half teaspoonful of baking soda, and one quart of water". . . . This may become the SIMPLEST AND MOST VALUABLE PRESCRIPTION IN HISTORY—the solution to be used orally for burns and other types of shock. It could fill the need in case of mass disasters when parenteral saline couldn't be given to all those affected. . . . It is said to be palatable. The exact prescription would read "3 to 4 grams of sodium citrate per liter of water, with baking

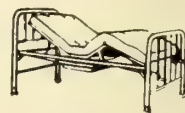
soda used in place of citrate when the latter is not available." . . . As much as 10 liters of this hypotonic solution may be drunk in 24 hours by an adult. . . . The idea is that of Rosenthal, but the recommendation has been made by the potent Surgery Study Section of the National Institute of Health to the Surgeon General.

It seems good to see the name 'Dr. Clarence G. Salsbury' as an author in the ARIZONA PUBLIC HEALTH NEWS. His retirement from the Ganado Mission led to fears that Arizona might lose him. . . . The January issue of the 'News' also contains an article by Dr. H. G. Crecelius on Biological Warfare. If anyone wants to have more details, and can find the January 1949 issue of ARIZONA MEDICINE, there is a long editorial which gives a summary—— up to date even now.

Theorists can make a treatment appear rose-colored. Then comes a realist, without the proper glasses, and the thing seems gray again. . . . After the hopeful reports of the salvage among narcotic addicts, Frank Sain, warden of the Chicago House of Correction, says "From my 30 years of experience I do not believe that there is a permanent cure for a confirmed narcotic addict." . . . Dr. Edward Helleher, who directs the Municipal Court's psychiatric institute, agrees. He lays the blame on a failure to follow up psychiatric treatment. The cause? Same old lack of psychiatrists and funds.

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SOMAPSYCHIC MEDICINE

LLOYD F. SMITH, M.D.

Monrovia, California

No doctor need ever suffer from boredom. Every patient that walks into his office will offer a tremendous challenge to his ability to diagnose and to treat a sick human being. And since humans are infinitely complex their illnesses can achieve a bewildering variety.

Yet beneath diversity three similar problems appear to underlie most sickness. Most patients will present physical signs, emotional reactions, and mental problems. For instance if a man comes in with a broken arm he may show us his crooked arm as a physical sign, worry about his job as an emotional reaction, and wonder about future use of his arm as a mental problem. In the same way a woman with a severe cough may have the cough as her physical sign, fear of tuberculosis as an emotional reaction, questions of how to get rid of her cough as a mental problem.

No wonder that doctors take for granted that we all have three more or less distinct parts,—body, emotions, mind. As a result scientists began to parcel out to specialists different bits and pieces to study. This schizoid program had curious results. Our universities turned out psychologists who analyzed our minds. Psychiatrists delved into and prodded around emotions. Plain doctors felt obliged to confine themselves more and more to patients' bodies.

After this folly reached its peak, there came a reaction. In the decade from 1930 to 1940 there gradually evolved a program to reassemble the pieces and treat human beings for what they are,—individuals. Even the word gives a clue, for individual in its original meaning means something not divided. So this new movement of trying to see the whole as well as the parts came into prominence, and took the name of Psychosomatic Medicine. The first journal devoted to Psychosomatic Medicine came out in 1939, and the first textbook in 1942.

If we come back to the three supposed parts that make up each of us,—body, emotions, mind, we get some idea of how complex things grow. We now have at least six relations to study. 1) How emotions react on the body. 2) How emotions react on the mind. 3) How mind affects the emotions. 4) How mind affects the body.

5) How the body influences our mind. 6) How the body influences our emotions.

In theory Psychosomatic Medicine would embrace all these six relations, unite them, and make us again individuals. In reality it failed to do so. Apparently that was too big an order for any one movement. What happened was that Psychosomatic Medicine confined itself for the most part to the first of the six relations,—how emotion reacts on the body.

So the bulk of work in Psychosomatic Medicine concentrates on such problems as the way emotions can bring about a duodenal ulcer or a rise in blood pressure. Or it deals with emotions in our choice as well as our digestion of food, emotions in asthma, emotions in migraine and so on.

Perhaps we err, but it would almost seem as if the very word 'Psychosomatic' exerts a tyranny of its own. Made up of two parts, psyche and soma, the psyche obviously takes precedence over the soma. The psyche roughly covers what we mean by emotions and mind, the soma refers to the body. Thus it may be more than coincidence that Psychosomatic Medicine looks at patients to see how emotions influence our bodies, not vice versa or how body influences emotions or mind.

Yet nothing is more certain than that body and mind are closely allied. The same goes for body and emotions. Defects of body can produce both emotional upsets and insanity. And in literal fact our food, both that during our prenatal state and that taken after birth until death, decides not only our physical health, but our emotional status and mental condition. It would seem that the next accent in medical lore might stress that prenatal and postnatal food has a decisive role in our physical development, and our physical state in turn rules much of our emotional and mental life.

The failure both of psychology and psychiatry to put enough attention on what we eat and what food goes to make up our body may explain some of their failures. Any real approach to a genuine preventive medicine must start with basic things like food, and the composition of our bodies. The well-known and often

quoted saying of Brillat-Savarin, "Tell me what you eat, and I will tell you what you are" (1) has more truth than humor.

We doctors will have to pay more attention to the tissues and food of mothers, before, during and after pregnancy. For in the prenatal period babies lay down the basic pattern of their bodies once and for all. After birth we continue to fill in the outlined sketches. Our building material in both instances is food. When the day comes that doctors generally will accept this obvious approach to preventive medicine the term 'Somapsychic Medicine' may serve them. In that term 'soma' or body comes before 'psyche' or the emotional-mental complex. Since we so often blindly follow the assumptions of language, as every student of semantics knows, the term 'Somapsychic Medicine' may keep reminding us where to start.

Non-medical writers at times appear to know the decisive role played by food. I know of no better example than Dana's "Two Years Before the Mast". On the voyage home Dana's ship had many cases of scurvy. Besides a masterful description of the physical signs of scurvy, Dana carefully says that victims of scurvy "lost all strength and spirit." Then after describing how they wolfed down raw onions and raw potatoes, or in advanced cases just the juice, Dana points out the change, both physical and emotional. "From lying helpless and almost hopeless in his berth, he was at the mast-head, furling a royal" after ten days on raw vegetables. (2)

Novelists too instinctively seem to know that food alters our actions. A classic example comes in Dostoyevsky's "Crime and Punishment." Raskolnikov, the main character, commits two murders. A friend, Svidrigailov, tries to console Raskolnikov's sister and to explain how such things could be. Svidrigailov gives one partial cause as "nervous irritability from hunger." (3) Besides this explicit statement, all through the book Dostoyevsky time after time shows that the murdered ate unwisely when he did eat, and often ate nothing at all.

Another overlooked instance of the relation of food to emotional and mental life can be found in all the higher religions. By higher religions we mean those that aim at a non-material or spiritual goal. Here we find many rules about food such as those in the Old Testament. (4). Yet most of these appear based on a

desire to set certain customs and habits for its members.

On the other hand most higher religions embrace a certain number of mystics. Mystics have been prominent in every higher religion from Bernard of Clairvaux and Francis of Assisi to the numerous Hindu mystics. Without exception mystics seem to agree in this, that they live on a deficient diet during the period of their mystical experiences. Mohandas Gandhi offers a recent example, with his long fasts alternating with longer stretches of marginal feeding.

Most admirers of mystics seem to take for granted that mysticism itself decreases the need for food. Yet another way of looking at the same facts might be equally valid, and capable of more scientific value. In the light of what we know of the effects of semi-starvation, may not mysticism itself be an effect of food lacking in quantity and quality? An interesting book could be written to give evidence that mystics get that way from inadequate diet.

Research on the effect of food in its relation to how we feel and how we think has lagged behind. Even so the little we do know gives an impressive amount of data that needs emphasis. The old tradition that mind dominates matter gains little support from modern science. As we watch how food rules the way we think and feel, our wonder grows that we neglect this viewpoint.

Cretinism affords a simple example. A cretin's birth is due in large measure to a lack of iodine during fetal life. Boyd describes him well. "The cretin is a dwarf physically and mentally. The mind, the skeleton, and the sexual organs do not develop. . . . He is a sad, old child . . . the pariah of nature, and all for want of a little iodine." (5). In this instance, at least, mental development fails along with the failure of an adequate amount of a simple food, iodine.

Pellagra shows us how a mind once sane can drift off into insanity, due to a defect of diet with its results of a sick body, emotional upheaval, mental imbalance. Pellagra also serves as an example wherein early treatment by proper food can cure body, emotions, and mind. Gaspar Casal, of Oviedo, Spain seems to have first discovered "Mal de la Rosa," now called pellagra. His book, however, did not see print until 1762. (6).

Meanwhile the Frenchman, Francois Thierry,

after working with Casal published his paper on pellagra in 1755. (7) And the Italian, Francesco Frapolli, followed with a paper in 1771 that both named the disease pellagra, and described it. (8).

Besides the physical signs, Thiery notes explicitly that pellagrins are "sad and melancholy . . . shedding tears and emitting cries without any object." Casal speaks of the way "heaviness . . . attacks them and causes them to give way to a sad crying." Frapolli goes into detail and writes, "Now the patients first begin to suffer in the head, anxiety, depression, sleeplessness, dizziness, cloudiness of mind . . . hypochondriacal delirium . . . and sometimes to suffer mania." Frapolli concluded "all then is in agreement in considering the bad food as the principal cause of the disease." He adds a wry postscript, "and then each accuses something else in the disease according to the customs of his country."

Today we have nothing to contradict and relatively little to add to what these pioneers discovered. Sebrell of the U. S. Public Health Service sums up the symptoms of pellagra. (9). Early pellagrins show nervousness, dizziness, headaches, fear. Later they hallucinate, make up wild tales, do not know where they are, cannot remember, get confused, fall into depression or rave in mania.

As Sebrell points out, the insanity of pellagra is the first mental disease known to come from poor diet, and curable in the early stages by improved nutrition. Sebrell suggested that possibly changes of the nervous system are due to a thiamine deficiency, while the mental changes may come from the nicotinic acid deficiency.

Turning to what we call emotional disturbances, Dr. Spies and his co-workers reported an interesting experiment. (10). They took 115 patients on a known deficient diet, but with no clinical signs. These 115 patients showed chiefly emotional upsets, such as fear, anger, hostility, depression, anxiety, and inability to pay attention or understand. Each patient got an injection of 50 mgm. of thiamine into a vein.

Within 30 minutes to 20 hours their 'emotional' symptoms subsided. The authors infer that such rapid change showed that no or minor structural change has occurred. They ran controls with injections of normal saline and found no results. They also found that the thiamine injections helped both those with known neurotic

backgrounds and those reasonably normal in previous medical history.

A more carefully controlled experiment has been reported by Dr. Wilder of the Mayo Clinic. (11) He isolated eleven women volunteers in a separate section of a mental hospital under complete control. These women had been previously hospitalized for mental illness and had got back to about normal. So each woman acted as her own control, since they knew her behavior for a long time before, during and after the experiment.

The eleven women had meals prepared to give less than one half a milligram of thiamine daily. Otherwise their meals sound fine, with plenty of beef, cheese, skim milk, fruit and vegetables. Also the volunteers got adequate Vitamins A, C and D, and considered B as brewers yeast. The brewers yeast was autoclaved to destroy most of the thiamine.

Every doctor sees many a patient who does not appear to eat half so well. Yet in a period of from 93 to 196 days every woman had to quit such a diet, since she could no longer eat it, or would vomit if she tried. Each woman in turn became irritable, depressed, quarrelsome, fearful, unable to concentrate, confused. None of these symptoms showed up at the start, but only after weeks on the diet. Thiamine restored to the diet without the patient's knowledge got rid of the symptoms.

From work like this Dr. Wilder inferred that the psychologic parts of pellagra and such deficiency diseases may come from a lack of thiamine. At least this seems certain. Inadequate diet shows itself very often by psychological symptoms. Both in animals and in humans often the first test of poor food may be abnormal behavior. Wilder goes so far as to suggest that if we tell a funny story and our patient fails to laugh we may suspect pellagra. To me this credits doctors with more skill in story telling than most of us can honestly claim.

Dr. Jolliffe and his associates reported 150 cases in which patients showed clouding of consciousness, cogwheel rigidity and strong reflexes to grasp and suck. (12). These scientists found that fluids and nicotinic acid reduced mortality and concluded that the syndrome showed a total lack of nicotinic acid.

Kreisler and others proved that to restrict the B complex vitamins induced severe primary mental changes in psychotic patients, or made

worse the existing psychotic trends. (13) They also believed that the kind of change depended on how restricted was the amount of B complex.

Up to the present most of the work on the relation of food to nervous and mental disease centers about vitamins, and especially about the vitamin B group. One report states that Vitamin E was tried out on random patients in institutions for chronic mental disease. (14). About 20% of patients showed clinical improvement, with best results in patients depressed, agitated, unable to express themselves in words.

Apart from vitamins the only other food substance tested for its relation to the mind seems to be glutamic acid. This amino acid roused interest after it was found to be the only amino acid metabolized *in vitro* by brain sections. On rats glutamic acid feeding seems to prove without effect. (15). Yet studies on humans have been done. Glutamic acid was given to 69 patients with convulsive disorders and varied degrees of intelligence. After one year 30 of these patients showed a gain of 11 points in I. Q. for the first six months, with no significant change after that. (16).

Another experiment on eight mental defectives reports great improvement by feeding about 10 gm. of glutamic acid daily for some months. (17).

When you review these and similar studies you soon begin to be impressed with this fact,—we have abundant evidence that how we feel and how we think bears some relation to what we eat. After this first reaction we next realize how comparatively insignificant is our knowledge of the relation. Most of what we know centers around the vitamins and how they affect us. The next step might well be one of total bewilderment. If food can exert such control not only on our bodies, but on our very emotional and mental health or disease, where do we get the courage to tamper endlessly with our food? Future historians may never cease to wonder how we in this day and age blithely process food though we know so little of what we are doing.

Even in the B group of vitamins, where relations of deficiency to mental and nervous disease are known, we have a gay abandon all our own. The cereals, and in our culture especially wheat, have long been a mainstay for the supply of B vitamins. Yet we have amazing skill in taking the natural B vitamins out of our flour products.

We salve our consciences by feeding these vitamins to animals. And then we put back into our flour a couple of synthetic vitamins and call such flour 'enriched'.

How do we explain this anomaly? No nation in history has been so overstocked with food for so long a time as we in America. Yet we all are not well fed. Only a doctor whose single criterion of food deficiency is death by starvation would fail to admit that the vast majority of patients we see, of all graduations of income, are poorly nourished. And like the Bible says of the number of fools, the number of neurotics is also infinite.

Some day we must call a halt. Food processing today has run beyond any sensible limit. The Roman army conquered its empire on a diet heavily dependent on wheat. A reincarnated Roman soldier might never recognize its modern equivalent, similar in name only, after it gets through its processing.

Wheat serves merely as an example. Sugar, processed from every trace of value except calories, rivals wheat as our modern fraud and curse. So it goes. Patients come to us who seldom, and at times apparently never, eat anything but processed food. We can ask if this be progress. Dr. Price (18) and others have shown beyond reasonable doubt that races of exceptional bodily health and nervous-mental stability have lived on unprocessed foods. These same races uniformly begin to deteriorate when they accept our processed foods of commerce, white flour, sugar and their countless combinations.

Medical practise grows more and more wrapped in the obvious. The skin specialist concentrates on his x-ray treatments and his lotions. Child specialists worry mostly about canned milk and canned food and shots against diphtheria, tetanus and whooping cough. Obstetricians go into a huddle about drugs to relieve pain instead of preparing women to reach the bodily perfection that might make childbirth a normal function.

Surgeons try to cut out or, with needle and thread, alter what we find objectionable. Internists with their needles want to improve our glands or restore organs beyond repair. Psychiatrists arrange our complexes into some kind of order, at times having to push and pull in order to fit them to their theories. We country doctors sit around and hope for the best, and

await the next antibiotic that will cure all ills of the flesh and spirit.

It begins to look to me as if we need a lot of change in medical practise. From my view of things the path appears something like this. We might start with the soil and begin to produce quality as well as quantity in our edible plants, and the same in our animals and animal products that we use for food.

Next we could call a halt on most types of food processing. We must abandon our present policy of allowing our foods to be processed to death. At the moment the whim of any company decides what to take out or what to add to our so-called foods. The only apparent limit to what a food processor can do seems to be what we can prove is actually poisonous. Right now we seem to act on the principle that we cannot ban any depletion of a natural food or the addition of any chemical to 'food' until many research men prove the change actually harmful. It was not until research proved that removing the hulls of rice killed and sickened countless humans that we even questioned this processing. We had to wait until 'butter yellow' was shown to produce cancer in animals to get this dye stopped. Not until 'agene' proved too well its ability to atrophy brain cells and kill dogs did we inquire as to its wisdom in flour for human use.

Some day we must put a limit to the advertising that persuades housewives to buy and feed us the food trash that fills magazine pages with its false claims. Or, failing that, we doctors must lift our timid voices in protest against all the hokum advertising about processed foods.

Finally we must begin to educate ourselves and our patients on what foods have real nutritive value, how to keep them in our homes, and how to serve them. Most of our families do at least as much harm to food once inside their doors as the combined skill of food processors along the way from farm to icebox. Cooking unwisely and too much has crippled far more of us than our automobiles have maimed.

If we grow our food better, do not tinker with it foolishly, but get it inside of us with a minimum of fussing, we certainly can improve our physical health. In any rational sort of preventive medicine, decent food for all of us must come first. After that we can count on a decrease in mental and nervous disease.

Should such a program ever appeal to enough

of the medical world we might call it 'Soma-psychic Medicine'. That would keep in mind that health of body must precede health of our emotional and mental life. The next fifty years may decide whether or not our nation and our way of life can survive. We had better start to look at the simple, obvious facts that concern our bodily-emotional-mental status. We could begin to pay more attention to our soil that provides our food, and the food that goes into our mouths.

Every nation that has come to grief in historical times has done so in part through some failure in its food supply. Generally this has been through soil depletion and erosion. By and large historians, a bookish lot, fail to see this. Even the learned Toynbee appears to miss it. (19). Yet Toynbee knows that the 'stimulus of new ground' has brought a surge of vitality, as in early America. But he rather gives this a mystical value rather than seems to realize that virgin soil provides unspoiled food, and unspoiled, abundant food offers health to body and emotions and mind.

Our land potentially can furnish abundance of food and of good quality. To tamper recklessly with food invites disease not merely of body, but of all that we are. In large measure we are what we eat, body, emotions, mind. Should we decide to continue in our present hit-and-miss fashion, with its tragic results, at least we should know what we are going, risking personal and national health. In the years of decision that await us, such a course appears to lead along a dangerous road.

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PERSONAL NOTES

Dr. Joseph M. Greer, Phoenix, spoke at the January 15th Staff Meeting of St. Joseph's Hospital on "Procurement of Medical Personnel." He attended as Arizona representative of the advisory board of selective service, a meeting held in Washington, D. C. January 12th and 13th. In essence he said that, according to present concepts, doctors would be eligible for service if they could stand up, could breathe, were warm, and were not expectorating tubercle bacilli.

Dr. Dermont W. Melick, Phoenix, took over the presidency of the Maricopa County Medical Society at the January 8, 1950 meeting, and outlined what he hoped to accomplish in the present year.

Drs. Wallace Meyer, and *Alfred D. Levick*, Phoenix, discussed a color-film on Anorectal Diseases at the January 29, 1951, Good Samaritan Hospital Staff meeting.

Dr. C. Thomas Read, Phoenix, presented an extremely interesting paper on "Usages of Streptokinase and Streptodornase" at the St. Monica's Hospital Staff meeting January 21, 1951.

Dr. Fred Holmes, Phoenix, presented "Medical Aspects of Cardiac Trauma" at the St. Monica's Hospital Staff meeting January 21st.

Dr. Daniel J. Condon, Phoenix, has left his practice, January 15, 1951, for Cambridge, Massachusetts where he will spend 18 months studying Forensic Medicine. He has been awarded a Research in Teaching Fellowship in the Department of Legal Medicine.

Dr. Arthur C. Carlson, who has been licensed to practice medicine in Arizona for many, many years, and who was formerly of Jerome and Cottonwood, and of the Yavapai County Medical Society, is now practicing in Phoenix, Arizona.

Dr. Clarence Salisbury, Phoenix, Chief of the Bureau of Preventive Medical Services, State Department of Health, has been appointed to the executive Board of the Cancer Detection Center St. Monica's Hospital. Other members are *Drs. Douglas Gain*, and *Thomas Woodman*, Phoenix.

At the February 5th Maricopa Medical Society meeting, the forthcoming Maricopa County Tuberculosis Survey was discussed from an organizational standpoint by *Dr. Lloyd K. Swasey*, Phoenix. *Dr. Simon Abrams*, of the U. S. Public Health Service discussed the expected

numbers of chest surveys (about 233,000) the expected numbers of active T.B. cases to be anticipated, the general mechanics of how the survey will be accomplished, and what the part of the Maricopa County Physicians will play in the study.

Drs. Rupert T. Rainey, Los Angeles, formerly of Phoenix, and *Dr. Howard Brown*, San Francisco, both renowned neurosurgeons, gave and discussed papers on "Lumbar Sympathectomy" at the Scientific session of the Maricopa County Medical Society February 5th.

Dr. Robert L. Maresca, formerly associated with the Veterans Hospital Papago Park, and then limiting his practice to anesthesia in Tucson, Arizona, has established a private practice of anesthesia now in Phoenix with *Drs. Benjamin Herzberg* and *Morris E. Stern*.

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Testimony of George F. Lull, M.D., Secretary and General Manager of the American Medical Association on Sec. 23 of S.1 (Amended) Before the Preparedness Sub-Committee of the Senate Armed Services Committee—January 30, 1951.

Mr. Chairman:

My name is George F. Lull. I am the Secretary and General Manager of the American Medical Association. I desire to submit the following statement in opposition to Section 23 of Senate Bill 1. I understand that other representatives of the Association will appear regarding some of the other features of this bill.

SECTION 23, S. 1, authorizes the President to socialize medical care and hospitalization for a large segment of the population by providing for the physical and mental rehabilitation by the Federal Government of registrants who are rejected for failure to meet standards for physical and mental fitness prescribed by the Secretary of Defense. This is a request by the Executive Department for vast new powers and federal expenditures in an area only remotely connected with defense. Here, in the guise of a national defense measure, is a new health proposal that surpasses, in the extent to which it nationalizes medicine, even the compulsory health insurance bills that have been introduced for so many years.

The American Medical Association thoroughly supports the concept that those individuals who cannot meet the physical and mental requirements of Selective Service should be rehabilitated, but it equally strongly opposes the idea embodied in Section 23 that this responsibility belongs to the Federal Government. It believes that such individuals should seek rehabilitation

from the many sources of medical and hospital care that already exist and that those sources can be mobilized in a voluntary way to provide the services necessary at a cost that registrants can afford.

The members of Congress are aware of the attitude of the American Medical Association toward the socialization of medicine and of the vigorous campaign we have waged to arouse public opinion to its danger. We have called the attention of Congress and the Nation to its exorbitant cost, its perversion of the physician-patient relationship, its regimentation of a free profession, the inevitability of political domination and interference in the field of medical care, the vagaries and administrative complexities inherent in the bills that have been proposed to establish it, the tragic experience of foreign nations where it has been attempted, the socialist and, often, communist associations of many of its sponsors and many other adverse characteristics. Over 10,000 organizations have seen fit to support the doctors in this struggle against socialism in a significant sector of American life, and the Congress, thanks to many members of this committee, has expressed the same vigorous attitude by refusing to support certain executive reorganization proposals that would have placed the would-be socializers of

medicine in a more strategic position from which to conduct their campaign.

The effort to utilize an important defense measure to promote a wide expansion of government medicine is a flagrant attempt to circumvent the will of Congress and of the people. It represents a disregard for public opinion that bodes ill for the future of our country and it must be prevented. If this extensive federal program costing billions of dollars is set in motion, it will eventually destroy the present framework of medical care that has placed the United States of America in its present enviable position among the nations of the world and replace it with a rigid, government controlled system.

The American Medical Association and its 53 constituent and 200 component societies stand ready to direct their resources to the development of a rehabilitation program for registrants with physical or mental defects that are remediable. We would be happy to cooperate with the Selective Service System and the Secretary of Defense in developing such a voluntary program, which would retain the present American system of medical care.

We urge the committee, therefore, to delete Section 23 in its entirety as unnecessary, costly in its activation and drastic in its implications.

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WOMAN'S AUXILIARY



MRS. A. J. BOSSE

President of Gila County Auxiliary

Mrs. Bosse is a native of Wisconsin and took her nurse's training at the Milwaukee County Hospital. She was married to Dr. Bosse in Wisconsin and they came to Arizona seven years ago. They have four children.

The Gila County Auxiliary held its first meeting in January at the Cobre Valley Country Club in Globe. They met at dinner with the doctors and each group held its individual meeting thereafter.

Much time was given to discussion of a gift to be given to the new Gila County Hospital and a committee was appointed to investigate.

Mrs. Clarence Gunter, Public Relations chairman, is to map out a public relations program to best suit the needs of the community and to begin work immediately.

Mrs. Charles Collopy was appointed legislative chairman and Mrs. Ira E. Harris, chairman of Today's Health. Four subscriptions to the publication were sold and the group has subscribed one hundred per cent to the Bulletin with thirteen subscriptions.

LEGISLATION

Substitute Senate Bill No. 1 has been introduced in the United States Senate and its con-

tents are of some concern to us.

In general this bill deals with universal military training, 18 year old draft, and sundry other "allied" subjects. It is to some of these latter sections that the American Medical Association has taken a definite stand because it believes that they are inimical to the best interest of our country. These are as follows:

1. The bill calls for a limit of 75,000 annual deferments for all classes of students. The American Medical Association feels that no specific limit should be set on student deferments, the figure should be left open so sufficient physicians and other professional personnel can be turned out to meet the country's actual needs, whatever they are determined to be.
2. The bill authorizes the President to provide for physical and mental rehabilitation of registrants who are rejected for failure to meet standards for fitness set by the Secretary of Defense. This covers medical or hospital treatment, including psychiatric care, in-or out-patient care, or other treatment, including necessary prosthetic devices. According to Dr. George F. Lull, Secretary of the American Medical Association, this is a request by the Executive Department for vast new powers and federal expenditures in an area only remotely connected with defense. Here, in the guise of a national defense measure, is a new health proposal that surpasses, in the extent to which it nationalizes medicine, even the compulsory health insurance bills that have been introduced for so many years.

By the time this is published it may be too late to write to your congressman, but if this bill has not already been passed it is important that you voice your opinion to your legislators.

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MEETING OF THE EXECUTIVE BOARD OF THE WOMAN'S AUXILIARY

The executive board of the Woman's Auxiliary to the Arizona State Medical Society met February 6, 1951 at the Hotel Westward Ho. The meeting was preceeded by a brunch. Highlights of the meeting are as follows:

To date, one hundred five Bulletin subscrip-

tions have been sold. This does not represent a sufficient number of subscribers as compared with membership, and it is hoped that more members will subscribe to this important and informative National publication.

Nurse's Loan reported that to date four girls have been given financial assistance—two beginning students, and two who are completing their training. This committee will begin to work immediately to secure new applicants.

Today's Health reports an approximate two hundred ninety-seven subscribers—work to continue to increase the number. Articles in the magazine are varied, interesting and authentic and it is hoped that those who subscribe will help to bring in other subscriptions. There are a number of gift subscriptions to public schools. Check was made on the schools and it was interesting to note the keen appreciation for the gift and the fact that the magazine was widely used. The membership is urged to further distribution of this excellent publication.

The Legislative chairman had prepared and sent to all County members and members-at-large for their information, a mimeographed report on the bills introduced and those approved by the State Society, in the 20th Legislature. She also sent word asking all women to write to their legislator immediately, urging the full appropriation of \$500,000.00 for the Children's Colony. Completion of the Children's Colony is a project the Auxiliary has been interested in for many years.

Inasmuch as the National Auxiliary is planning to compile complete histories of all State Auxiliaries, the Historian requested each county publicity chairman to gather together such material immediately and submit it to her. She asked for cooperation so that she can meet the National date and also have the State file up-to-date before convention.

State convention was discussed—Mrs. Joseph M. Kinkade of Tucson, appointed chairman. Tentative convention dates for Auxiliary activities are set for April 29, 30, May 1 and 2, 1951. Convention news will follow in Arizona Medicine and via special bulletin. The National Auxiliary President, Mrs. Arthur Herold, has accepted an invitation to attend convention, and Mrs. Herzberg urgently requested that all members make plans to attend convention sessions.

Those who attended the board meeting were: Mrs. Benjamin Herzberg, Mrs. Royal Rudolph,

Mrs. Delbert Secrist, Mrs. Brick P. Storts, Mrs. George Enfield, Mrs. Joseph Kinkade, Mrs. Louis Hirsch, Mrs. Joseph Ehrlich, Mrs. Archie Cru-thirds, Mrs. Donald Carlson, Mrs. James R. Moore, Mrs. Roy Hewitt, Mrs. Karl Harris, Mrs. Carlos Craig, Mrs. Jesse Hamer, Mrs. Thomas Bate, Mrs. R. Lee Foster and Mrs. Harry Southworth.

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THE AUXILIARY TO THE MARICOPA COUNTY MEDICAL SOCIETY

The Auxiliary to the Maricopa County Medical Society held its February meeting in the Nurses' Lounge at Good Samaritan Hospital.

Mrs. Royal W. Rudolph, president-elect of the State Medical Auxiliary, gave a report on the 1950 mid-winter conference in Chicago, and discussed the highlights of national work.

Following this, Dr. Lloyd Swasey reported on the coming Maricopa County Chest X-Ray Survey. He introduced Mrs. Margaret Casoon who talked on the nurses' work in connection with this, and Mrs. Olga Welsh who discussed the social work. Dr. Simon Abrams, of the U. S. Public Health Department, gave the results of previous surveys and told what might be expected of this one. Mrs. Karl Harris, president, asked that members of the Auxiliary volunteer to help with the survey in each of the eight districts.

In the absence of Mrs. Donald Polson, chairman for Red Cross in the Auxiliary, Mrs. Jesse Hamer announced that the Red Cross drive had started, and that again this year the doctors were being approached by members of the auxiliary for their contributions. Last year participation was tripled and the amount contributed was doubled.

Mrs. Karl Harris read a letter from the Y.W.C.A. telling of a course they will soon present . . . a study of all the welfare agencies in the city. They would like to enroll some representatives from the Auxiliary.

At the conclusion of the meeting, Mrs. John Findley, hospitality chairman, introduced four new members: Mrs. Raymond Huger, Mrs. David Long, Mrs. Alloys Tallakson, and Mrs. Donald Victor.

Refreshments, in the Valentine theme, were served by a committee headed by Mrs. William A. Bishop.

PIMA COUNTY NEWS

The January meeting of the Pima County Medical Auxiliary met at the home of Mrs. Royal W. Rudolph. Hostesses for the evening were Mmes. F. G. Leseman, Jr., Louis Hirsch, Henry Limbacher, Edward Hayden and C. E. Bensema.

The Auxiliary group canvassed the doctors for contributions to the Community Chest and Mrs. Kenneth Baker announced that they had gone over their quota.

One Hundred Dollars was contributed to the school health council for its revolving health fund, and twenty-five dollars was voted to the visiting nurse service for medicines.

Mrs. Royal Rudolph, President-elect of the State Auxiliary, reported to the group on the Seventh Annual Conference for State Presidents and Presidents-elect, held in Chicago. Her report was enlightening and interesting.

Committee reports were given.

FEBRUARY REPORT OF PIMA COUNTY MEDICAL AUXILIARY

Mrs. Benjamin Herzberg of Phoenix, State President of Woman's Auxiliary to the Arizona Medical Association, was guest of honor Tuesday, February 13, 1951 of the Pima County Medical Auxiliary at a luncheon at the Tucson Country Club. Mrs. Herzberg gave a most interesting and inspiring talk making us all more determined to be better informed Auxiliary-wise.

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Mrs. James R. Moore of Phoenix, State Historian, also attended the luncheon.

Hostesses included: Mrs. Delbert Secrist, Chairman, Mmes. Joseph Kinkade, Donald Schell, Donald Lewis, Stuart Sanger, William Carrell, James Sickler, Jackman Pyre, Michael Bernfeld, and George Shetter.

While in Tucson, Mrs. Herzberg conferred with Mrs. Joseph Kinkade, Convention Chairman, on plans for the State Convention to be held in Tucson April 29, 30, and May 1 and 2. Margaret Flood, Pima County Publicity Chairman.

YAVAPAI COUNTY AUXILIARY

The Woman's Auxiliary to the Yavapai County Medical Society met for dinner at the Hassayampa Country Club January 11th. Mrs. Benjamin Herzberg, state president, and Mrs. Royal Rudolph, state president-elect, were honored guests during the evening.

Mrs. James H. Allen, president, announced that fifteen dollars, seven baskets of food, canned milk, and twenty three packages of toys were given to the Salvation Army at Christmas time.

Plans were made for the annual rummage sale to be held February 15, 16, 17, at the Woman's Club House. Mrs. Joseph McNally was appointed chairman.

Proceeds from a bridge and canasta party will be given to the Nurse Loan Fund.

There were twenty three present for dinner and the business meeting. Two guests were wives of doctors serving with the armed forces.

Everyone enjoyed hearing Mrs. Herzberg and Mrs. Rudolph, both of whom brought us news from the national, state, and county auxiliaries.



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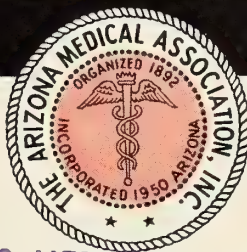
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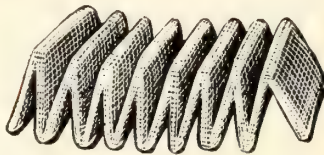
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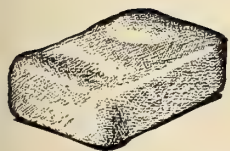


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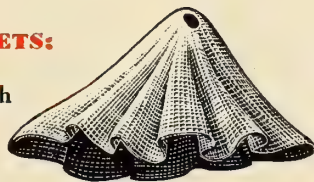
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1. Thewlis, M., and Gale, E. T.: Ambulatory Care of the Aged, Geriatrics, 5:331 (Nov.-Dec.) 1950.

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ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 4



APRIL, 1951

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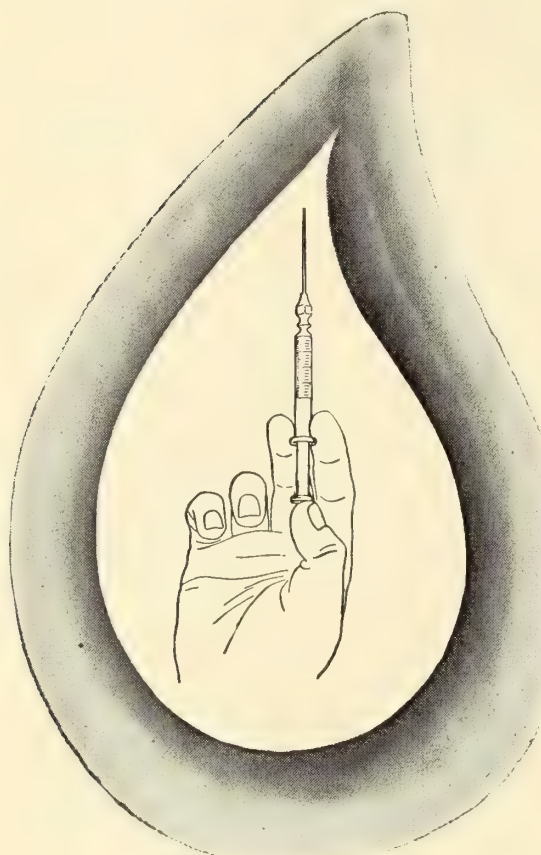
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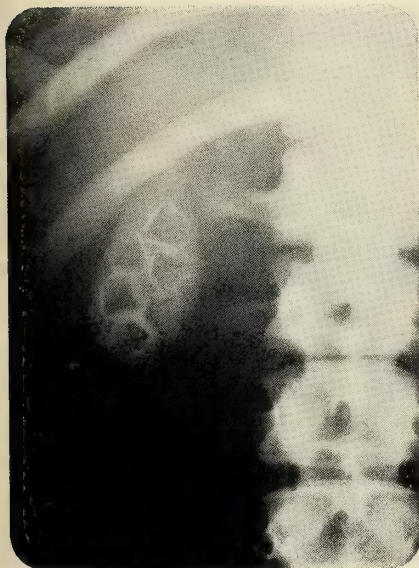


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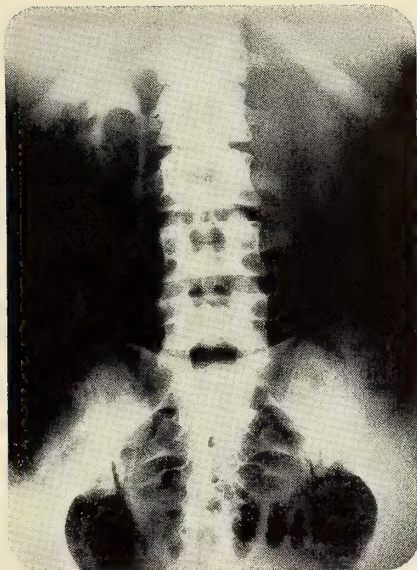
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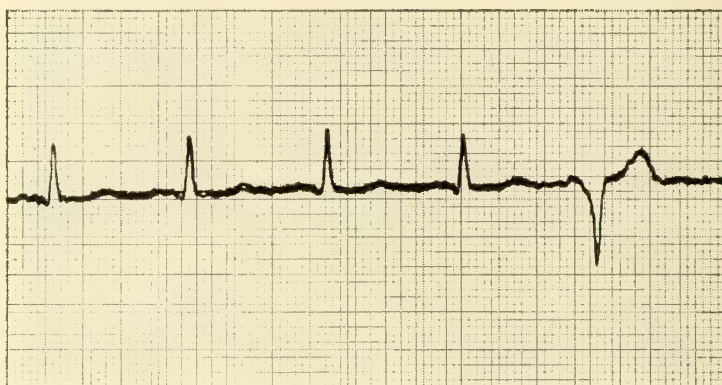
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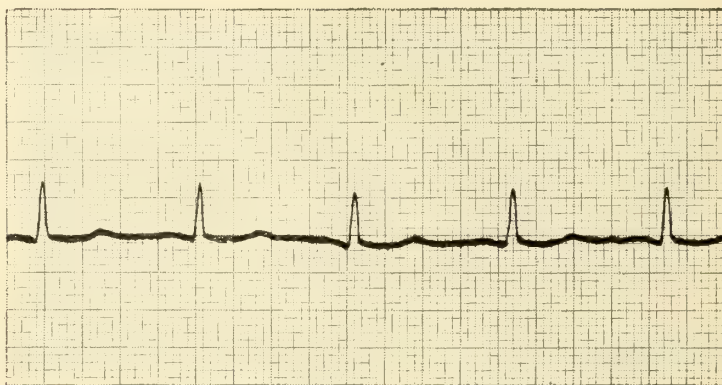


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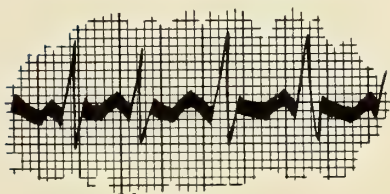
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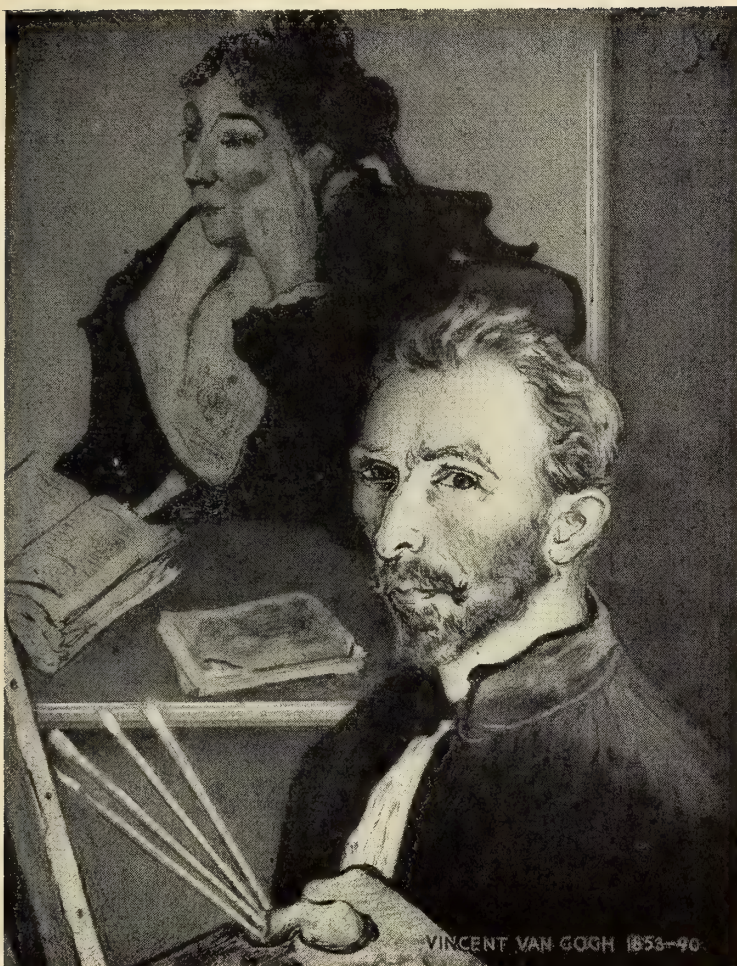
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	ORGANISM	NO. OF CASES	RESULTS		
			GOOD*	EQUIVOCAL	POOR
No organic or obstructive disease					
	B. coli	15	14	1	0
	A. aerogenes	4	4	0	0
	Aerobic diphtheroids	3	2	1	0
	S. albus	2	2	0	0
	Aerobic non-hemolytic streptococcus	2	2	0	0
	Ps. aeruginosa	1	0	1	0
With organic or obstructive disease					
	Ps. aeruginosa	3	1	0	2
	P. vulgaris	1	0	1	0
	A. aerogenes	1	1	0	0
	TOTALS	32	26	4	2

Douglas, R. G.; Ball, T. L., and Davis, I. F.: California Med. 73:463 (Dec.) 1950

*“A good result was recorded when in 72 hours or less the temperature fell to normal, the pyuria cleared, a negative culture was obtained and the patient was symptom-free.”

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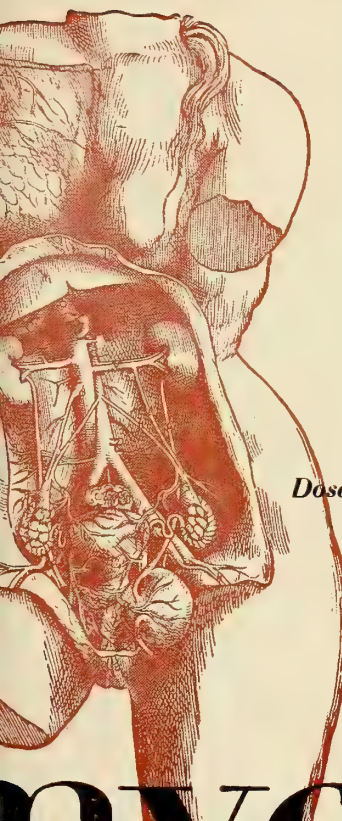
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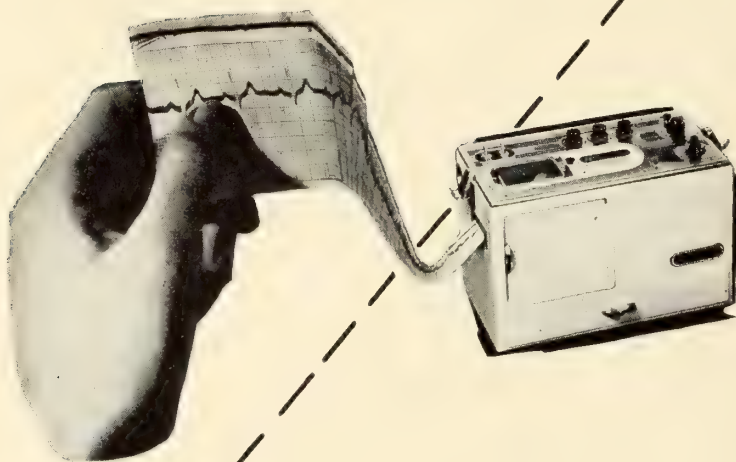
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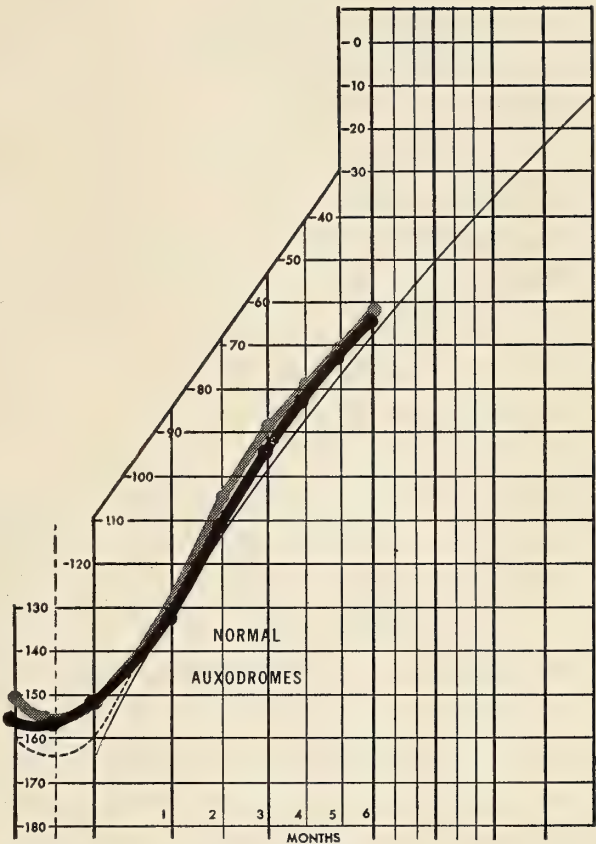
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Growth data, recomputed on Wetzel Grid, based on "selected subjects, most of whom were favored by environment;"² age: from birth to 6 months.

- 1. Wetzel, N. C.: J. Pediat. 29:439, 1946.
- 2. Jackson, R. L., and Kelly, H. G.: J. Pediat. 27:215, 1945.



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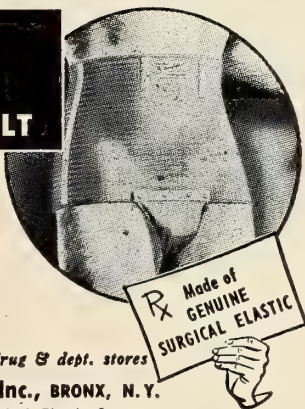
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Nervous tension and chronic anxiety, discharged through a labile Autonomic Nervous System, can cause somatic disturbance.^{1,2} Such states may involve any one of the organ systems or several at one time.^{1,3} The outline below is designed to relate gastrointestinal and cardiovascular symptomatology to the exaggerated response of the autonomic nervous system.

	Physiologic Effects of Autonomic Discharge	
	Sympathetic	Parasympathetic
Gastro-intestinal System	Hypomotility Intestinal Atony Hyposecretion Reduced salivation	Hypermotility Gastrointestinal spasm Hypersecretion
Cardio-vascular System	Rapid heart rate Peripheral vasoconstriction	Slow heart rate Vasodilatation
Functional Manifestations	Palpitation Tachycardia Elevated blood pressure Dry mouth and throat	Heartburn Nausea-vomiting Low blood pressure Colonic spasm

The data here tabulated is from references 3,4,5,6,7, given below.

When the clinical picture is suggestive of functional disorder, the diagnosis is supported by the presence of the following indications of autonomic lability:

Variable Blood Pressure
Body Temperature Variations
Changing pulse rate
Deviations in B. M. R.
Exaggerated Cold Pressure Reflex
Oculo-Cardiac Reflex Abnormalities
Glucose Tolerance Alterations

Therapy in these cases is directed toward: 1) relieving the somatic disturbance to prepare the patient for psychotherapy*; 2) guidance in making adjustment to stressful situations and correction of unhealthy attitudes.

*Drug treatment using adrenergic and cholinergic blocking agents in conjunction with sedatives.^{8,9,10.}

1. Ebaugh, F.: Postgrad. Med. 4: 208, 1948. 2. Wilbur, D.: J.A.M.A. 141: 1199, 1949. 3. Williams, E. and Carmichael, C.: J. Nat'l. Med. Assoc. 42: 32, 1950. 4. Goodman, L. and Gilman, A.: The Pharmacological Basis of Therapeutics, The Macmillan Co., 1941. 5. Katz, L. et al: Ann. Int. Med. 27: 261, 1947. 6. Weiss, E. et al: Am. J. Psychiat. 107: 264, 1950. 7. Alvarez, W.: Chicago Med. Soc. Bulletin, 581, 1950. 8. Rakoff, A.: A Course in Practical Therapeutics, Williams and Wilkins, 1948. 9. Karnosh, L. and Zucker, E.: A Handbook of Psychiatry, C. V. Mosby Co., 1945. 10. Harris, L.: Canad. M.A.J. 58: 251, 1948.

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Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 4



APRIL, 1951

TREATMENT OF CHEST EMERGENCIES—MEDICAL ASPECTS

ROGER O. EGERBERG, M.D.

Los Angeles

A discussion of the treatment of medical emergencies of the chest in a fifteen minute period will necessitate the compendium approach. In most instances, the important thing about treatment is the consideration of all the possible diagnoses. I am, therefore, discussing a rather complete list of such emergencies. As far as the actual treatment is concerned, I have tried to limit myself to the emergent treatment; in other words, that part of the treatment which should be instituted almost automatically, after which one could sit down to give thought to the problem.

For the purposes of this talk, I am assuming the following definition of a medical chest emergency:

SLIDE 1

MEDICAL CHEST EMERGENCIES

Definition: Symptom complexes within the chest, arising slowly, rapidly or suddenly, in which the physician sees the patient at a time when treatment must be instituted immediately—such treatment being in the field of medicine.

It is impractical to group these emergencies according to symptoms. They are, therefore grouped anatomically.

SLIDE 2

LOCATION OF MEDICAL CHEST EMERGENCIES

- I. Pleura and lungs
- II. Mediastinum
- III. Heart
- IV. Vessels
- V. Diaphragm
- VI. Brain

We shall take up all these headings and list

the emergencies that might occur in each anatomical group.

SLIDE 3

I. PLEURA & LUNGS

- A. Bronchial Asthma
- B. Spontaneous Pneumothorax
- C. Pneumonia
- D. Pulmonary edema due to inhaled gases
- E. Hemoptysis
- F. Emphysema

Now the treatment of these emergencies:

SLIDE 4

A. Bronchial Asthma

- Rx. 1. Intravenous fluids—5% glucose in water (saline)
2. Aminophyllin—I.V.
 3. Epinephrine—I.M.—I.V.
 4. Oxygen—catheter—mask—tent
 5. Sedative? Never morphine

Bronchial asthma is an emergency more often than we realize and in spite of the frequent talk to the contrary, people do die in their asthmatic attacks. Those that become severe emergencies usually do so after being in a state of chronic asthma for weeks or months. They are almost always emotionally upset, either due to their long-continued air hunger or their emotional difficulties may be the primary cause of their asthma. They have not been able to eat nor drink, are very much dehydrated and have probably had fairly large amounts of adrenalin over a period of months. Intravenous fluids are, therefore, placed first on the list of treatments. If they have been vomiting and sweating a lot, this should be normal saline; if they have not, 5% glucose is preferable as they can use the food in addition to the water.

Aminophyllin can be given directly into the tubing of the intravenous set. If the patient has been taking epinephrine for weeks or months, but at a constant dosage, say 0.5 c.c. of 1-1000 solution, the doubling or tripling of this dose

Read before the Physicians Chest Disease Symposium, Los Angeles, California, January, 1950. From the Medical Service of Wadsworth General Hospital, Veterans Administration Center, and the Department of Medicine, School of Medicine, University of California at Los Angeles.

Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

may well give dramatic relief, or the same dose the patient has been taking without effect may give relief if given intravenously instead of intramuscularly. As soon as possible, oxygen by mask, catheter or tent should be administered.

If the patient is much wrought up, a sedative is important, but ordinarily, the patient has been without sleep for some period of time and a slight relief of symptoms will allow him to relax and go to sleep. While morphine is one of the best sedatives for emergent conditions in general, it is strongly contra-indicated in asthma because of its depressant effect on the respiratory center. I have seen at least three patients die as a result of receiving a quarter of a grain of morphine during a severe attack. It relaxes them and markedly slows their respirations at a time when they should be struggling for breath. Therefore, one of the quicker acting barbituates is the sedative of choice

SLIDE 5 B. Spontaneous Pneumothorax
 due to: Ruptured emphysematous bleb
 or Ruptured pleural adhesion or Visceral pleura needle tear
 Resulting in:
 Atelectasis
 Shift of mediastinum
 Rx: Needle intercostally on side of pneumothorax

Most cases of spontaneous pneumothorax are not dire emergencies, though they are frightening to the patient; however, a small portion whether they be due to ruptured emphysematous blebs or to torn pleural adhesions, may become extreme emergencies because of the great and rapid shift of the mediastinum that can occur. To this group, one should add those occasions where a needle has been inserted into the chest for diagnostic or therapeutic purposes and has cut a half moon in the visceral pleura. In these instances, the small pleural nick may act as a valve opening on inspiration and closing on expiration, thus allowing air to pass through the bronchus into the pleural cavity but not back. This pump-like action can compress the lung completely and can displace the mediastinum toward the opposite side, partially compressing the opposite lung and placing enough torsion on the great vessels to embarrass not only respiration but circulation.

If such occurs, the immediate and urgent treatment is the insertion of a needle, preferably about 18 calibre, into the thorax on the

side of the pneumothorax. This will allow the air under pressure to come out. It is important to remember that the valve effect will exist and this needle may have to be left in place for 24 to 48 hours. A piece of rubber from a rubber glove may be tied over the adapter end of the needle loosely so that it will act as a valve, counter-acting the pleural valve, allowing air to come out of but not to enter the pleural cavity. Such a patient should be watched closely for re-accumulation of the pneumothorax until the pleural wound is healed

SLIDE 6 C. Pneumonia

- Rx. 1. Antibiotics—large doses
- 2. Parenteral fluids
- 3. Oxygen
- D. Pulmonary Edema due to Inhaled Gases
- Rx. 1. Epinephrine
- 2. Oxygen

Occasionally one sees a pneumonia for the first time when the patient is in extremis or almost so. Bacterial studies may or may not be available, but the patient very likely has a pneumococcal septicemia in addition to his pulmonary involvement. Large doses of antibiotics are indicated immediately; oxygen as quickly as it can be obtained and parenteral fluids as quickly as they can be started. Penicillin is still the antibiotic of choice in most bacterial pneumonias, the exceptions being tuberculous pneumonia and pneumonia due to Friedlanders bacillus. These two infections are most susceptible to Streptomycin. 600 thousands units of procaine penicillin twice daily is an adequate dose for a patient with pneumococcal pneumonia and bacteremia (and this would include 95% of desperately ill pneumonia patients). 5 million units of aqueous potassium penicillin daily would be necessary if the pneumonia were due to a staphylococcus. If marked improvement has not occurred in 24 hours, streptomycin and sulfadiazine therapy should be instituted; streptomycin dosage being 0.5 grams every 6 hours and sulfadiazine 4 grams initially followed by one gram every 6 hours. With the advent of the broader spectrum antibiotics such as aureomycin, chloromycetin and terramycin comes the possibility that these may prove to be the antibiotics of choice in pneumonias of unknown etiology. Aureomycin and terramycin can be given intravenously and the dosage is 500 mg. every 12 hours for either of these drugs.

Occasionally, chemically irritating gases may be inhaled to the point of giving pulmonary edema. Such was the case in an eastern clinic disaster, following the explosion and burning of their file of old type X-ray films. The pulmonary edema was sudden and severe though delayed, and accounted for many of their deaths. It can occur in a sudden severe exposure to sulphur dioxide fumes or chlorine or other gases used commercially.

Treatment consists of administration of epinephrine and oxygen under positive pressure.

SLIDE 7 E. Hemoptysis

- Rx. 1. Rest—sandbags
- 2. Morphine
- F. Emphysema
- Rx. 1 Oxygen

Usually, hemoptysis is a real emergency to the patient—more than it is to the physician. However, it needs quick and careful handling to minimize its after effects and occasionally to save a life. This consists of absolute rest with the affected side held in a slightly lower position than the unaffected. Sandbags or soft heavy objects should be used to immobilize this side. The reason for keeping the affected side lower is to prevent insofar as possible the accumulation of blood in the non-affected side. Toward this end, the usual position for postural drainage may be indicated. Morphine will allay the patient's fears, quiet him and slow down respiration. However, it must be used judiciously, being careful not to abolish or severely depress the cough reflex. If the bleeding continues, it may be necessary to institute pneumothorax on the affected side.

The patient with severe emphysema, with a vital capacity of less than 1000, has very, very little pulmonary reserve and may become an emergency under situations which would hardly disturb normal people. A cold, a slight asthmatic attack, irritating atmosphere causing coughing, or a fever may indeed make a severely emphysematous person a desperately ill person. Oxygen is the primary treatment, but remember that a severely emphysematous patient takes to oxygen as to a drug. He quickly becomes dependent upon it psychologically and once started, he wants to be near it the rest of his life.

There are the emergent situations due to pathology in the mediastinum.

SLIDE 8 II. MEDIASTINUM

- A. Tumor with vena caval pressure
- B. Mediastinitis
- C. Emphysema
- D. Sudden gross shift
- E. Ruptured esophagus
- F. Status thymicolymphaticus

SLIDE 9

- A. Tumor with vena caval pressure (usually lymphosarcoma or Hodgkin's group)
 - 1. X-ray
 - 2. Nitrogen mustard
- B. Mediastinitis
 - 1. Antibiotics
- C. Emphysema
 - 1. Expectant
 - 2. Antibiotics

A tumor of the mediastinum: sarcoma or lymphosarcoma, is obviously not an emergency if noticed early, but a doctor may not be called until the time when the pressure has reached the point where either the superior vena cava or the inferior vena cava is very much obstructed. There will be severe venous distention in the upper or lower or both parts of the body, and with little blood returning to the heart the pulse will be weak and rapid. The only help that can be given aside from oxygen is a rapid destruction of the tumor mass. This has to be accomplished by x-ray or nitrogen mustard. On the whole, nitrogen mustard acts more quickly but its effect does not last as long.

Mediastinitis can be due to several causes, the most common being infected hilar glands that have ruptured into the mediastinum. Other possibilities would include penetration of infected material from the esophagus. Treatment is immediate institution of antibiotic therapy and the choice of antibiotics rests with the decision as to whether it is a ruptured tuberculosis gland, a pyogenic infection or leaking esophagus.

The treatment of emphysema of the mediastinum is primarily expectant. Such an emphysema will probably be associated with emphysema in the upper part of the thorax. The pressure is not likely to become dangerous, but with air in the tissues, infection may result and penicillin or other antibiotics should be used prophylactically.

SLIDE 10

- A. Sudden Gross Shift (due to pneumothorax)
 - 1. Treatment of pneumothorax

- B. Ruptured Esophagus
 - 1. Expectant
 - 2. Surgical
- C. Status thymicolymphaticus

Sudden gross shift of the mediastinum grave enough to become an emergency is due to sudden pneumothorax which has been discussed.

Ruptured esophagus: The treatment of a ruptured esophagus is primarily surgical and I believe Dr. Byron will discuss it with you. However, it may occur during gastroscopy if the patient has a carcinoma that involves the upper end of the stomach. We had one such patient at our hospital and he was treated with antibiotics and in a sense, expectantly. He recovered from the small tear and resultant mediastinitis rather uneventfully.

Status Thymicolymphaticus: If there is such a condition, and there are many who believe so, the only treatment is preventive and consists of x-ray therapy directed toward the thymus when it is found to be large. The emergencies unfortunately consist of finding the infant dead.

SLIDE 11 III. HEART

- A. Coronary Occlusion
- B. Acute Heart Failure
- C. Cardiac Tamponade
- D. Steering wheel injury
- E. Elevated Blood Potassium level
- F. Low Blood Potassium level
- G. Paroxysmal (supraventricular) Tachycardia

Although the heart is in the chest, it may not have a place in this chest symposium. It must, however, be considered in the differential diagnoses and a chest emergency will certainly include many instances where the heart is the major organ at fault, so it will be considered briefly.

SLIDE 12

- A. Coronary Occlusion
 - 1. Rest
 - 2. Morphine
 - 3. Oxygen
 - 4. Papaverine
 - 5. Anticoagulants
 - 6. Small blood transfusions

The primary treatment in coronary occlusion is aimed at resting the heart, improving its blood supply if possible, and theoretically at least, at the prevention of the spread of the thrombus. Bed rest is probably more complete if the upper part of the body is propped up to an angle of 30 degrees or so. Morphine is important for re-

lief of the pain, to help control the shock and to allay the anxiety associated with the attack. Oxygen will make the circulating blood more efficient. There is some argument as to the use of coronary vessel dilators, one school feeling that dilation may cause considerable slowing down of the blood flow to create further thrombus formation; the other school believing the larger the vessels are, the better the heart will be nourished and the smaller the dead, infarcted area will be. According to your choice, Papaverine, Aminophylline and Atropine may be used. Anti-coagulants have been urged upon us rather strenuously during the past three or four years and I still think if I had a coronary occlusion, I would like to receive anti-coagulants; however, this pendulum will start swinging back after a while and one might hazard the guess that five years from now they will be used cautiously and in moderation.

If the occlusion is due to hemorrhage under a small plaque in one of the coronary vessels, it is difficult to see how an anti-coagulant could do anything but harm. If it is due to a thrombus within the vessel, its indication would seem obvious. If a primary occlusion is followed in a day or two by a secondary one, anti-coagulants are indicated, as this suggests an extension of the clot. Heparin acts immediately; dicumarol may take a day or two to produce its effect. Dicumarol should not be given if the prothrombin time cannot be followed carefully.

Recent studies indicate that associated with the shock seen in severe coronary occlusion, there is a decrease in blood volume. Small transfusions are, therefore, useful in combating this state, and if the shock is severe, these transfusions should be given arterially rather than venously.

SLIDE 13

- B. Acute Heart Failure
 - 1. Phlebotomy
 - 2. Oxygen
 - 3. Digitalis parenterally or I.V.
 - 4. Morphine
 - 5. Aminophyllin
- C. Cardiac Tamponade (in pericarditis)
 - 1. Pericardial tap
- D. Steering Wheel Injury
 - 1. As coronary occlusion

If a patient in acute heart failure has pulmonary edema, an emergency exists. Ascites or ede-

ma in the extremities or sacral region is not an emergency. In moderate to severe pulmonary edema, a phlebotomy is indicated even if it is found necessary to give a transfusion again at a later time. A so-called tourniquet phlebotomy or bloodless phlebotomy, the placing of a tourniquet high on each of the four limbs, is a procedure which can be done quickly and easily and which often produces dramatic results. It will perhaps suffice of itself and will at least give an indication of the usefulness of a real phlebotomy.

Oxygen is again important. Immediate adequate digitalization of the patient parenterally or intravenously is likewise important. Morphine in small amounts will bring about real rest and relaxation, and again, vaso-dilators are useful. I prefer Aminophyllin but most of the younger men in our hospital seem to prefer Papaverine.

Associated with pericarditis, one must always keep in mind a pericardial effusion; weak, distant heart sounds, weak rapid pulse and low pulse pressure are indications pointing towards this condition.

The treatment is of course the removal of the effusion immediately by pericardial tap.

Following a mild collision, the driver of a car usually receives a fairly severe blow on his chest from the steering wheel. This can, without fracturing the ribs, produce a contusion of the heart which will give electro-cardiograph changes similar to those found in a coronary occlusion. The treatment of this condition is essentially the same as that of a mild to moderate coronary occlusion, with an adequate period of rest. The prognosis of course is different for there is not necessarily an implication of diseased blood vessels, and the patient need not expect a recurrence.

SLIDE 14

- E. Elevated Blood Potassium
(Due to severe depletion of chlorides)
 - 1. Saline solutions
- F. Low Blood Potassium
(At end of Diabetic Coma)
 - 1. Potassium chloride I.V.—slowly
- G. Paroxysmal (supraventricular) Tachycardia
 - 1. Vagal Stimulation
(danger in older people)
 - 2. Morphine I.V.
 - 3. Quinidine

In severe renal disease with salt depletion through the kidneys, potassium may be pulled out of the cells and be found present in the blood in dangerously high amounts. A bizarre electrocardiogram is produced, usually showing markedly deformed QRS complexes and T waves and little inconspicuous P waves. This can end in cardiac arrest. The main treatment if any is to replace as quickly as possible the lost sodium chloride to enable the potassium to return to the cells.

At the end of a diabetic coma when the acetone has disappeared from the urine and blood sugar levels are normal or approaching normal, and one expects the patient to do well, occasionally patients will suddenly take a turn for the worse and die. In this instance, the potassium in the blood has gone into the cells with the glucose and with the aid of dilution has left the blood level too low. Ten grains of potassium chloride given intravenously over a period of a half an hour should not throw the patient into the hyperkalemic state and should correct the hypo-kalemic state.

Paroxysmal supraventricular tachycardia may at times become an emergent state. You are all familiar with the immediate means of controlling this by vagal stimulation, such as massage of the carotid sinus and pressure on the eyeball. With people over 50, this method should be used with extreme caution as it occasionally produces a hemiplegia, sometimes permanently. When it is used, only one side at a time should be stimulated. If the attacks are frequent, quinidine or digitalis should keep them under control, but if they occur at intervals of approximately a year, it is more logical to treat them as they occur. Morphine intravenously can relieve these attacks rapidly but does not do so consistently.

SLIDE 15 IV. BLOOD VESSELS

- A. Pulmonary embolism
- B. Dissecting Aneurysm
- C. Ruptured Aneurysm
- D. Ruptured Esophageal Varix
- E. Fat Embolism

SLIDE 16

- A. Pulmonary Embolism
 - 1. Papaverine
 - 2. Oxygen
 - 3. Anticoagulents
 - 4. Search for source
- B. Dissecting Aneurysm

1. Morphine
2. Rest
- C. Ruptured Aneurysm
 1. Morphine

Pulmonary embolism is too often thought of as a fatal complication of an operation. It is however, a fairly common occurrence following thrombophlebitis, phlebothrombosis, endocarditis, carcinomatosis, etc. The size of the embolus and its location determines the outcome. However, in borderline cases, certain emergent measures may be instituted. Because there is edema associated with the obstruction of the vessel, there is room for rapid improvement if the patient can be tided over with oxygen and vasodilators. The second step is directed towards the prevention of further emboli either by use of anticoagulents or venous ligation.

In dissecting aneurysm, the odds are very much against both the patient and the physician. However, patients have lived for years following a dissection and it is always possible that the final dissection may be into the main trunk of the vessel rather than out through the adventitia, so treatment should be given.

Treatment should aim at rest and keeping the blood pressure down, and toward this end, morphine is about the most useful drug.

A ruptured aneurysm is invariably fatal; however, the pain is excruciating and morphine is certainly indicated in large doses while it is rupturing.

SLIDE 17

- D. Ruptured Esophageal Varix
 1. Pressure on varix
 2. Morphine
 3. Transfusion
 4. Surgery
- E. Fat Embolism
 1. 50% glucose
 2. Purified Albumin
 3. Adrenalin
 4. Oxygen

If the patient lives long enough, the treatment of a ruptured esophageal varix will certainly fall into the field of surgery, and I am sure Dr. Byron will cover it. There are, however, two or three procedures that the first physician to arrive on the scene should institute. If the blood pressure is still up, morphine should be given. Transfusions are indicated for replacement purposes. If a Miller-Abbott Tube with bag is available, this should be passed into the

stomach, the bag blown up and the tube retracted thus exerting pressure on the esophageal gastric junction, which is the region of most frequent hemorrhage. We have had five experiences in our hospital where the bleeding was brought under control by that method. Topical thrombin may be used in association with this.

Fat embolism is a diagnosis well worth remembering and the second thing to remember about it is that it is apt to present itself clinically three days after the fracture which precipitated it. This is due to the fact that the fat itself often does not obstruct enough vessels to cause respiratory embarrassment, but on breaking down into fatty acids it produces edema which adds to the pathologic picture and causes acute respiratory embarrassment, or in the case of the brain, coma. 50% glucose, purified albumin, adrenalin—all are agents aimed at combatting the edema. Oxygen will help combat the anoxemia that must result from this obstruction to the smaller arteries.

SLIDE 18

V. THE DIAPHRAGM

- A. Rupture through of a subdiaphragmatic abscess
 1. Postural drainage
 2. Suction
 3. Antibiotics

VI. THE BRAIN

- A. Hysteria
 1. Treat the family first

There are a number of chest emergencies associated with the diaphragm, but they come primarily under surgical emergencies of the chest. However, the rupture through of a subdiaphragmatic abscess, such as an amoebic liver abscess might be considered a medical emergency. If small, it may occur with very little distress to the patient. If large, the patient will certainly become alarmed over the amount of pus that he is forced to cough up.

Both postural drainage and suction will help to remove this pus and antibiotics are certainly indicated to prevent a secondary pneumonia.

The Brain: I place this organ in the present category because when I was in practice, about half of the so-called medical chest emergencies on which I was called out were hysterias. If it is a simple case of hyperventilation with tetanic contractions, the picture may be obvious, but don't belittle the power of the emotions in simulating organic disease, and if you feel it is hysteria, treat the family first.

CLIMATE AND RHEUMATIC DISEASES*

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The relationship of climate to rheumatic diseases has received attention of many investigators. Certain studies during and after the war have clarified some of the problems of the effect of climate on one of the rheumatic diseases—Rheumatic Fever. In this paper, some of these studies will be reviewed. Also to be reported is a survey of the incidence of Acute Rheumatic Fever among the resident and native** population of a Southwestern city. From this area the incidence of recurrences of Rheumatic Fever will be presented. For these purposes, data were received from the following sources: (a) Six physicians—four Pediatricians and two Internists, (b) The Veterans Administration Hospital, and (c) The Federal Prison Camp, all in the same locality.

Two other rheumatic diseases, Rheumatoid Arthritis and Degenerative Joint Disease will be considered. Reports on the effect of meteorological changes on 112 cases of Rheumatoid Arthritis and 34 cases of Degenerative Joint Disease will be summarized. Further observations of the incidence of acute and chronic Rheumatoid Arthritis in the native and resident population, based on a study of 659 cases will be reported.

I. RHEUMATIC FEVER

Rheumatic Fever will be considered first, because in this disease, there appears to be no doubt that the effect of climate, the incidence of Hemolytic Streptococcic infections and other etiological factors are closely related. Interesting reviews (1, 2) have appeared concerning the effect of geography and climate on predisposing factors, governing the incidence of Rheu-

matic Fever. Comparisons were made of the hospital admission rates and analysis of necropsy material from various cities. Table I exhibits the incidence of Rheumatic Fever or Rheumatic Heart Disease in children, based on hospital admissions. It is noted that the percentage falls from North to South. A similar difference in the incidence of Rheumatic Heart Disease based on necropsy studies is exhibited in Table II. Comparisons were also made of the incidence of Rheumatic Fever among comparable groups during the last war. It became evident that marked differences exist between the frequency of Rheumatic Fever in the North as compared to the South. Also certain areas, the Rocky Mountain area, the Great Lakes and the Midwest Area exhibited a high incidence as compared to a low incidence of the South.

Since Southern Arizona is an area of low incidence of both Group A, Hemolytic Streptococcic infections and Rheumatic Fever, the results of the following survey may be of interest. The survey reported by six physicians (3, 4) included: (a) Acute Rheumatic Fever arising in the native and the resident population and (b) All cases of Rheumatic Fever. These findings are condensed in Table III.

The number of Acute Rheumatic Fever patients was reported as follows: One, two, eighty, twenty, zero and two cases. The times of observation were three, five ten, ten, eleven and eleven years respectively, thus over a total period of fifty years, one hundred and five acute Rheumatic Fever patients were seen among the native population.

Recurrent Rheumatic Fever reported by the same physicians was as follows: recurrences were noted in one, zero, forty, zero, five and

TABLE I
THE PERCENTAGE INCIDENCE OF RHEUMATIC FEVER OR RHEUMATIC HEART DISEASE, IN CHILDREN*, BASED ON HOSPITAL ADMISSIONS

City	Percentage
Philadelphia	5.8%
Portland, Oregon	3.5%
Cincinnati	2.7%
Dallas	0.8%
Los Angeles	0.69%

*From Rheumatism and Arthritis, Ann. Int. Med. Jan. 1948
*Presented at the first Arizona Regional meeting of The American College of Physicians at Phoenix, October 22, 1949.
**Native—defined as a lifetime resident.

TABLE II

THE INCIDENCE OF RHEUMATIC HEART DISEASE BASED UPON NECROPSY STUDIES*			
City	Total Cases	Rheumatic Heart Disease	Percentage of Total
Boston	8,300	456	5.5
Atlanta	1,754	61	3.5
Galveston	2,463	22	0.9
New Orleans	16,121	102	0.63

*From Rheumatism and Arthritis, Ann. Int. Med. Jan. 1948

two cases or a total of forty-eight recurrences out of 1,141 cases studied. The recurrence rate was 4.2 percent for this series. No chemical prophylaxis was used.

The Veterans Administration Hospital (5) reports (Table IV) for a period of twenty-one months, January 1948 to October 1949, a total of 2,938 admissions, 147 or five percent were rheumatic diseases, of this number, one or 0.68 percent were Acute Rheumatic Fever and two admissions or 1.36 percent (both for the same patient) were recurrent Rheumatic Fever.

Finally, from the Federal Prison Camp, (4) a work camp, no cases of either Acute or Recurrent Rheumatic Fever were observed among 6,000 inmate admissions over a period of thirteen years.

From this review and these observations, it appears that the following remarks are warranted: one, that the incidence of Rheumatic Fever is related to both meteorological factors and geographical location; two, that Acute Rheumatic Fever occurs in the area reported but it is of low incidence; three, that Acute Rheumatic Fever appears to be less frequent in the natives, as compared to the other residents. These differences observed may be due to factors other than those that relate to climate and location; four, that since recurrences of Rheumatic Fever are frequent, i.e. an estimated eighty-five percent in children and fifty percent of all cases, the low percentage reported here appears to be due to conditions characteristic of the area and five, that the reported absence of Rheumatic Fever among prisoners apparently is related

to environment in addition to geography and climate.

II. RHEUMATOID ARTHRITIS

Next, Rheumatoid Arthritis will be considered in relation to climate. There is again an abundance of material available in the literature. (1, 6) First a patient's ideas about weather and arthritis may be of interest. A patient who has had a Rheumatoid Arthritis and who has written an excellent book* for patients with the disease states, "There are few medical subjects about which there is more misinformation or lack of understanding, than the effect of weather upon arthritic sufferers. Unfortunately, some medical practitioners seem to believe that in a warm, dry climate, improvement or recovery from the disease without medical aid is possible, even likely. My research supports no such view. Good weather alone will cure no ones arthritis! That arthritics become increasingly uncomfortable both mentally and physically with the approach of cool, damp, cloudy weather, but feel better when warm, dry, sunny weather returns, is a fact well known to anyone who has had this disease or has associated with many who do. The simple facts about the effect of weather upon arthritis should be made available to millions who suffer with the disease. Arthritics who can continue to live in a warm, dry, sunny climate and who intelligently and determinedly work for recovery under able medical management, seem to enjoy greater physical and mental comfort, make better progress, and have the best chances of recovery."

Observations on the effect of meteorological changes on patients with Rheumatoid Arthritis.

*Managing your Arthritis, Dorrance & Company, Philadelphia 1947.

TABLE III
REPORT OF PHYSICIANS EXHIBITING THE ACUTE RHEUMATIC FEVER OBSERVED IN NATIVE AND RESIDENT POPULATION AND THE NUMBER OF RECURRENCES

Reporting Doctor	Time of Observation	Acute Rheumatic Fever		Recurrences Noted on All Cases
		Natives	Other Residents	
J. R. Sickler	3 years	1	25	1
M. Semoff	5 years	2	25	0
B. P. Storts	10 years	80	400	40
H. C. Thompson	10 years	20	400	0
P. W. Holbrook	11 years	0	280	5
H. E. Thompson	11 years	2	11	2
Totals	50 years	105	1141	48

Recurrence Rate Percent 4.2, all cases.

are summarized in Table V. You will note that out of 112 chronic rheumatoid arthritic patients, ninety-two or eighty-three percent were subjectively worse with meteorological change, while nineteen or seventeen percent were not.

Observations of the incidence of Acute and Chronic Rheumatoid Arthritis among the native population may be reported as follows: in a review of 659 private patients with Rheumatoid Arthritis, only one native or lifetime resident appeared in this series with a Chronic Rheumatoid Arthritis. Acute or Subacute Rheumatoid Arthritis in natives was seen in four patients of the same series.

Observations on the effect of climate alone on Rheumatoid Arthritis. In this same series of 659 patients no permanent remission of a Chronic Rheumatoid Arthritis, due to climate alone, was observed. Several patients appeared who were markedly benefited.

These observations indicate that since approximately eighty-three percent of the Chronic Rheumatoid Arthritics are affected adversely by meteorological change, these are the patients who will be subjectively improved in a warm, dry climate. They are more amenable to treatment in such a climate. This group particularly are the patients in whom a change of climate may be indicated. Investigators in Sweden (7)

have noted the beneficial effect of a controlled "hot dry microclimate" in patients with Rheumatoid Arthritis.

These observations also indicate that the extremely low incidence of both Acute and Chronic Rheumatoid Arthritis, among the native population is related to climate, geographical and other undetermined factors.

Again that since remissions in Rheumatoid Arthritis, due to climate alone are rare, medical management is essential. It is essential since in a previous study (8) of 345 patients with Rheumatoid Arthritis, it was found that approximately sixty percent had deformities, most of them preventable, which occurred during the time the patients were not under medical care. Unfortunately many patients are now waiting for the "NEW DRUGS" before seeking such care. They should understand, as all patients should with Rheumatoid Arthritis, that without proper supervision, progression of the disease and crippling are likely to occur.

III. DEGENERATIVE JOINT DISEASE

Degenerative Joint Disease will be briefly considered. Most of the things that were observed concerning Rheumatoid Arthritis apply to Degenerative Joint Disease. The effect of climate on these patients is shown in Table V. Listed there are thirty-four cases of Degenerative

TABLE IV
THE INCIDENCE OF ACUTE AND RECURRENT RHEUMATIC FEVER BASED ON HOSPITAL ADMISSIONS* FOR TWENTY-ONE MONTHS

	All Cases	Rheumatic Diseases	Acute Rheumatic Fever	Recurrent Rheumatic Fever
Total Admissions	2938	147	\$	2 (same Patient)
Percentage of Total Admissions		5%	0.034%	0.068%
Percentage Total Rheumatic Diseases		100%	0.68%	1.36%

*Veterans Administration Hospital, Tucson, Arizona. January 1948—October 1949.

TABLE V
THE "WEATHER SENSITIVITY" IN 112 PATIENTS WITH CHRONIC RHEUMATOID ARTHRITIS AND 34 PATIENTS WITH DEGENERATIVE JOINT DISEASE

Disease	No.	Weather Sensitivity			
		Yes		No	
Rheumatoid Arthritis	112	93	83%	19	17%
Degenerative Joint Disease	34	30	88%	4	12%
Totals	146	123		23	

Joint Disease. Thirty or eighty-eight percent were definitely sensitive to weather changes, while four or twelve percent were not. A warm, dry sunny climate appears to be beneficial, particularly in those patients who are weather sensitive. The benefits derived from this type of climate seem to be subjective in character, therefore a comprehensive medical plan of treatment (9) should be followed in these patients with Degenerative Joint Disease.

CONCLUSION

In conclusion it has been pointed out that all three of these rheumatic diseases, Rheumatic Fever, Rheumatoid Arthritis and Degenerative

Joint Disease have some relationship to climate.

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BALL THROMBUS OF THE MITRAL VALVE

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Ball thrombus of the heart is mentioned so frequently as a complication of mitral stenosis that one is surprised in looking at the literature to find so few authentic cases reported. Still less often has the correct diagnosis been made ante-mortem. Evans (1) discusses a case and submits photographs of the pathologic specimen. Abramson (2) in his very exhaustive monograph of 1924 collected only 19 cases from the literature of ball thrombi and added a case of his own. David Spain (3) reported a case in which a correct ante-mortem diagnosis had been made. Kaplan (4) reported an immense pedunculated thrombus in one auricle, 7 x 9 x 5.5 cms. in size, attached to the lateral wall over a 2.5 x 1.2 cms. area and almost completely covering the mitral valve.

During 1949 I made such a diagnosis ante-mortem, which was proven by an autopsy. In 1950 I saw another case, almost identical clinically, in which an autopsy, unfortunately, could not be done.

After reviewing the literature, because of the apparent rarity of this striking clinical entity, the following two cases are reported.

CASE ONE

Miss Helen A., nurse, aged 37 years, who had had acute rheumatic fever in 1939, was first seen by me on November 20, 1947 with severe cardiac decompensation and auricular fibrillation. An electrocardiogram showed extreme right axis deviation with tremendous ST2-3 covering and inversion suggestive of extreme coronary insufficiency. A standard cardiac regimen

was followed and she gradually improved. On December 16, 1947 she suddenly developed symptoms of a cerebellar lesion. She was admitted to a hospital and given dicumarol, quinine, papaverine, digitalis and mercurhydrin. The cardiac status appeared to be well compensated. On March 12, 1948 she was asking if she could resume work because she felt fine.

The pulse rate was 64 per minute and the apex rate 72 per minute. There was no cardiac dilation. After careful restudy she was permitted to begin working half days to determine what she could tolerate. On March 20, 1948 she got up to go to the bathroom and suddenly collapsed, falling to the floor unconscious. I saw her one-half hour later in typical extreme cor pulmonale, completely unconscious and deeply cyanotic. In view of the clinical picture, a diagnosis of a ball-valve thrombus obstructing the mitral valve was made. She was taken to a hospital, where she expired that evening. At the autopsy the mitral orifice was shrunk to "about the size of radial artery" and was occluded by a "ball thrombus about 4 x 1 x 1 cm., firm, and surface uniformly smooth and glistening." In the auricular appendage there was a roughened area from which the thrombus had become detached to lodge in the extraordinarily narrowed mitral orifice.

CASE TWO

Mrs. Anne W., aged 25 years, was first seen on September 27, 1949 giving a history of having had rheumatic carditis at the age of 15 years. A therapeutic abortion had been performed two

years previously because of the heart condition. There was a marked double murmur heard at the apex. The basal metabolic rate was plus 43 per cent. The erythrocyte count was 3,130,000 per cu. mm. An electrocardiogram showed a marked right axis deviation-sinuss rhythm, rate only 85, and the PR interval was .20 seconds. She was given propyl thio-uracil, iron and liver tablets, hi-caloric diet, and rest. On October 19, 1949 her weight was 107 pounds and the erythrocyte count was 4,370,000. On November 13, 1949 the basal metabolic rate was minus 19 and murmur was much less harsh. On December 27, 1949 her weight was 103 pounds, so she was again given propyl thio-uracil. The heart was essentially unchanged from the last examination. She was cheerful, happy about her job and feeling quite well, planning "a big time for New Year's Eve."

On January 6, 1950 at 6:30 A. M. she arose as usual to get ready to go to work. She collapsed suddenly in the bathroom as she was putting on make-up. Her sister picked her up and dragged her to bed. When I saw her a short time later she presented the typical pic-

ture of extreme cor pulmonale. She was rushed to the hospital with a tentative diagnosis of ball thrombus. A bronchoscopic aspiration of the edema fluid was done, 100% O₂ was given plus all the usual stimulants, but to no avail and she went into anoxic shock and respirations ceased at 3:00 P. M. but the heart beat for another five minutes. An autopsy was not performed. However, I have no doubt in my mind that this case clinically is identical with the first case. The syndrome is unique in its dramatic onset and, once seen, it can never be forgotten.

COMMENT AND SUMMARY

Two cases of ball-thrombus of the mitral valve are presented. Only one, however, was absolutely proven by autopsy. The literature is briefly summarized. It seems that the paucity of cases previously reported may be due to failure to recognize this syndrome. The essential clinical features are presented.

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BASIC SCIENCE SEMINAR

THE METABOLISM OF CHOLESTEROL WITH SPECIAL REFERENCE TO ATHEROSCLEROSIS

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Presented at the Basic Science Seminar, Tucson Medical Center
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The purpose of this paper is to summarize the few known facts and the multitude of theories concerned with the metabolism of cholesterol, with special reference to its relationship to atherosclerosis. Limited time necessitates the omission of some interesting yet unessential material as well as the abbreviation of some more important data.

The presentation of this subject is timely as recent experimental work has given promise of a better understanding of the metabolism of cholesterol and a potential basis, perhaps, of a means to combat the great killer, arteriosclerosis.

The subject will be discussed in relation to a diagram (Fig. I) showing the passage of cholesterol through the body, including sources, metabolism within the body, and excretion.

First, however, an understanding of the nature of the compound, cholesterol, is needed.

CHEMISTRY OF CHOLESTEROL

General Considerations—There is in nature a large group of chemically related compounds called *steroids*. These include the sterols, of which cholesterol is a member, the bile acids, cardiac aglycones, sex hormones, adrenal cortex hormone, antirachitic vitamin D, saponins, toad poisons, and certain carcinogenic compounds. The steroids have as the basis of their chemical relationship the cyclopentanophenanthrene nucleus.

The *sterols* are specifically those steroids which have the characteristics of a monohydroxy alcohol. The term *sterol* is derived from the Greek, *steros*, a solid, and *ol*, an alcohol. Thus,

Exogenous—Diet—Since only those foods of animal origin contain cholesterol, we need not concern ourselves with a discussion of other food substances. It should be noted, however, that the plant sterols have chemical reactions very similar to those of cholesterol and that older food tables, which list cholesterol in vegetable fats probably are in error because of such reactions. It was once thought that animals were able to transform plant sterols into cholesterol, but it now is recognized that plant sterols are not absorbed by the body.

The cholesterol content of various foods is given in Figure III. From these data we note that eggs, oysters, butter, and the organ meats contain the greatest amounts of cholesterol on a mgm. per 100 gm. basis, while whole milk has an insignificant amount. However, to get a true picture of dietary intake, one must refer to the mgm. of cholesterol in average portions of foodstuffs. Thus we see that milk may become a more significant factor in cholesterol intake. Eggs, although still a potent factor, are brought far below the levels of beef brains and hearts. However, eggs are consumed much more frequently by most people.

Endogenous—Synthesis—The work of Chanon (1) and that of Randler and Knudson (2) first showed that rats maintained through two or more generations on a sterol-free diet had significant amounts of cholesterol in their bodies, and accumulated more during growth. Since then, other investigators have confirmed the synthesis of cholesterol in the animal. It was shown that a man on a low-sterol diet excreted a greater quantity of sterols than he had ingested. Heavy hydrogen (deuterium) studies have indicated not only the synthesis, but also the basic substances from which the body builds the cholesterol molecule.

Rittenberg and Schoenheimer (4) showed that the cholesterol of mice fed heavy water contained D_2 in proportions indicating that it had replaced one-half of the hydrogen atoms. They concluded that cholesterol was synthesized from small molecules, perhaps those formed in the intermediate metabolism of fats and carbohydrates. Studies by Bloch and Rittenberg (5, 6) indicate that acetic acid was such a small basic molecule. They labeled sodium acetate with D_2 , and later with both D_2 and radioactive carbon and recovered cholesterol with these labeled atoms present in both nucleus and side chain. They also demonstrated (7) that any compound which yielded acetic acid during its metabolism contributed to cholesterol synthesis.

The site of the synthesis of cholesterol appears to be in the liver, but other organs have been given credit for this process. These include the adrenals, spleen, thyroid, pancreas, and pituitary. It has been suggested that cholesterol is formed, not by one organ, but by cells of the reticulo-endothelial system. Bills, after consideration of all facts, states that endogenous cholesterol probably originates in the cells in which it is found (8). It has been estimated that approximately 300 mgm. of cholesterol may be synthesized daily by the body.

The endogenous cholesterol is excreted into the small intestine via the bile and intestinal secretions in the form of free cholesterol. To this endogenous cholesterol in the gut is added the cholesterol of the ingested foods, which also is almost completely in the free form.

ABSORPTION OF CHOLESTEROL

The absorption of sterols from the gut is of an extremely discriminate nature. As a small change in structure gives a vastly different physiologic activity to a sterol, so does it render a sterol absorbable or unabsorbable. For example, allocholesterol, a mixture of isomers, and dihydrocholesterol, a saturated form, are excreted almost completely, in the feces (9). Vegetable sterols can not be absorbed by animals. Sitosterol given to rabbits was recovered quantitatively and unchanged in the feces (9). It is of interest that the provitamin D, ergosterol, like other plant sterols is not absorbed, but the active, irradiated vitamin is taken up by the body.

Within the lumen of the small bowel the cholesterol is almost entirely in the free state. That in the thoracic duct is both free and esterified. It follows that the process of absorption

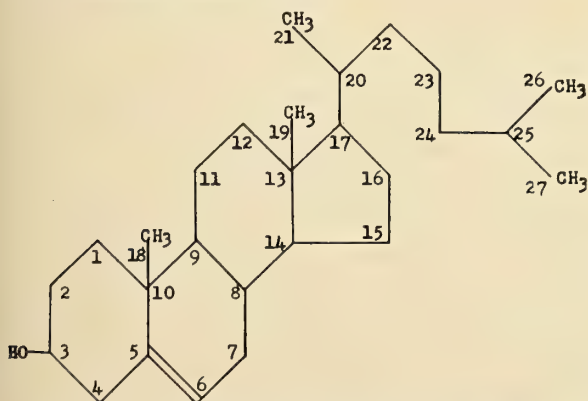


Figure II: Structural Formula of Cholesterol.

entails esterification of a portion of the cholesterol. Mueller prepared pancreatic extracts which were capable of esterifying cholesterol (10). The responsible enzyme, pancreatic cholesterase, is markedly activated by the bile acids, cholic acid and glycocholic acid, esterifying cholesterol with fatty acids, particularly the highly important unsaturated fatty acids (11). Experiments on bile-fistula dogs have shown that bile is not indispensable for cholesterol absorption. However, fat and pancreatic enzymes are essential. Cholesterol administered to animals on a fat-free diet was recovered quantitatively in the feces (12).

Cholesterol esters enter the epithelial cells of the intestine while free cholesterol is poorly, if at all, absorbed. Some cholesterol must be released from its esters during passage through the intestinal wall, however, since the ratio of free to esterified cholesterol is approximately the same in thoracic duct lymph as in blood, regardless of the state of the ingested sterol.

Many investigators have shown that most of the absorbed cholesterol enters the lymph, but the passage of a portion directly into the portal blood cannot be denied. The rapid rate of removal of cholesterol from the blood, especially by the liver, makes for difficulty in tracing its course. Regardless of the route, the cholesterol eventually finds its way to the blood stream and it is this blood cholesterol that is of prime importance in the pathological changes associated with its metabolism.

CHOLESTEROL IN THE BLOOD

The absorption of cholesterol esters probably is only of minor importance in considering those mechanisms by which fatty acids enter the body. Some short chain fatty acids pass directly into the intestinal mucosa. The rest are phosphorylized in the wall of the intestine to phosphatides, lecithin in particular.

Gubner and Ungerleider (13) stress the importance of a consideration of all of the mechanisms of fat absorption rather than that of cholesterol alone. They call attention to a remarkably constant concentration and division of the various lipid fractions in any individual, suggesting a dynamic interdependence and relationship. This is particularly true of the ratios, cholesterol:cholesterol esters, and cholesterol:phospholipids. Clinically, such interrelationships are important in that one must consider lipid metabolism as a whole rather than cholesterol levels alone. The constancy of these ratios lies in the ability of the liver to regulate the transfer of fatty acids to cholesterol and phosphatides.

The high concentration of hydrophobic, insoluble cholesterol in the blood stream is due to agents which carry it in colloidal suspension. Hydrophilic phospholipids may aid in this. Weak bonded lipo-protein complexes are of more importance. Alpha₂ and beta-globulin fractions of serum protein, as well as gamma globulin and albumin, contain both cholesterol and phospholipids in high concentration. This

Food	Cholesterol mg./100 g.	Average Portion	Weight Gm.	Cholesterol mg./Av. Portion
Butter	280	2 pats	14	39
Cheese, American	160	1 slice	28	45
Cod Liver Oil	400	1 tsp.	4	16
Eggs, white	0	1	35	0
Eggs, yolk	2000	1	17	340
Milk, whole cow's (4% fat)	12	1 glass	210	24
Salmon	60	1 c. canned	113	68
Oysters	230-470	6	113	260-531
Shrimp	150	8	68	98
Beef	125	¼ lb.	113	141
Pork	70-105	¼ lb.	113	79-119
Veal	140	¼ lb.	113	158
Chicken	60-90	¼ lb.	113	68-102
Brains, beef	2360	¼ lb.	113	2667
Heart, beef	2110	¼ lb.	113	2384
Liver, calf	360	¼ lb.	113	407
Sweetbreads	280	1 c.	113	316

Figure III: Cholesterol Content of Foods. (3)

globulin-lipid bond may be broken by heparin, forming a protein-heparin compound.

Cholesterol is present in both blood plasma and cells, as it is a normal constituent of all body cells. The amount in the erythrocytes is less than that of the plasma, but on the basis of water content of both, the distribution is equal. Average values for plasma cholesterol range from 130 to 240 mgm. %, and the percentage of this in the free state, a physiological constant under normal conditions, ranges from 20% to 40%.

Such values for cholesterol levels are termed "average" rather than "normal" since there is much variation under so-called "normal" conditions. All of the factors involved are not known at this time, but studies have shown that age and sex are two important influencing factors. Keys (14) correlated age and cholesterol levels in 541 adult males who were free of detectable disease (Figure IV). He demonstrated that there was a progressive rise in total cholesterol levels with age. A plateau was reached at ap-

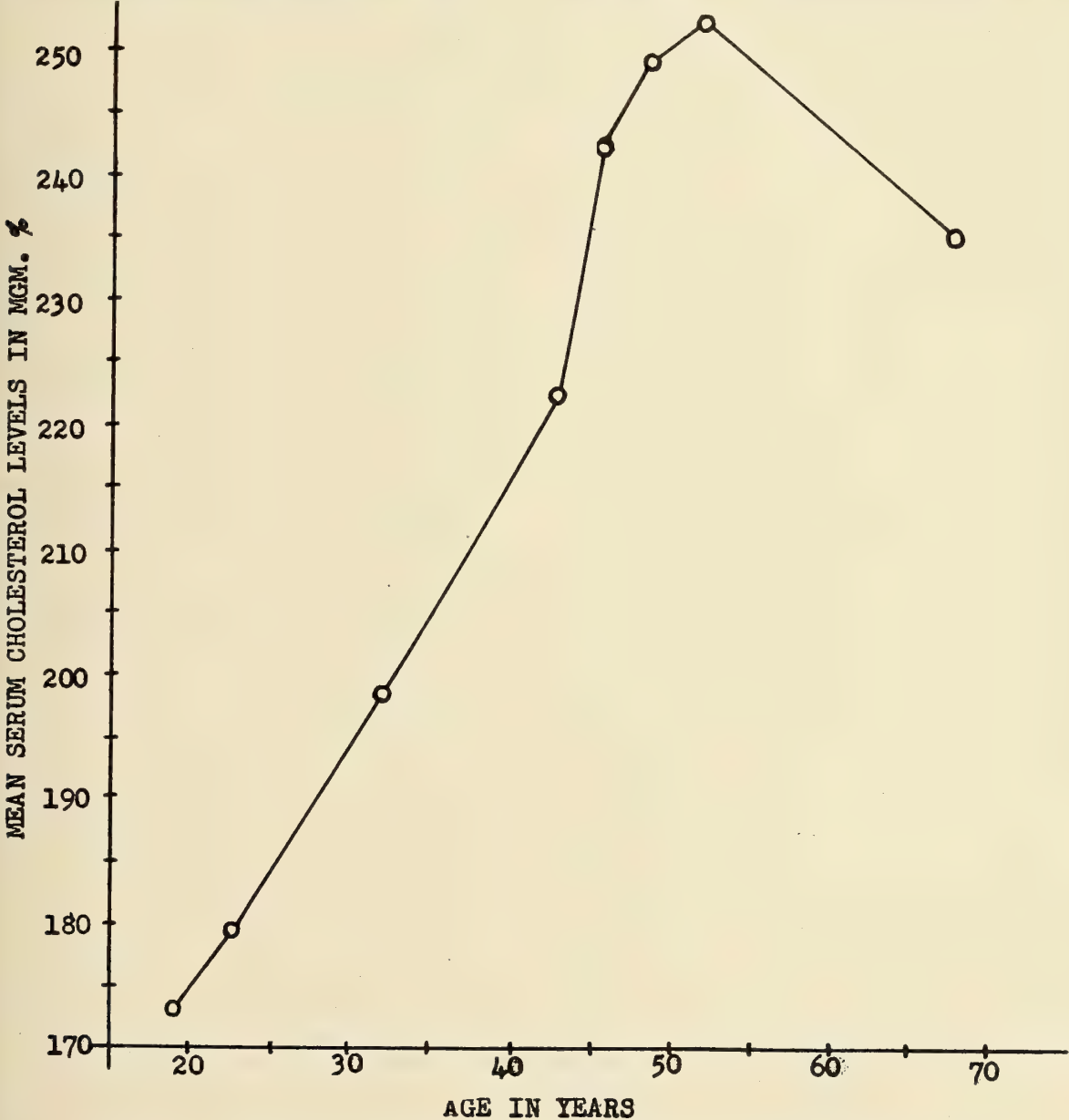


Figure IV: Total Serum Cholesterol Levels at Basal Rest. "Normal" Males. (14)

Age groups: 17-20, mean-19	45-47, mean-46
21-25, mean-22.5	48-50, mean-49
27-35, mean-32	51-55, mean-52.5
39-44, mean-43	63-74, mean-68

proximately 50 years of age, and a slight decline occurred in persons of sixty years. It also has been demonstrated that at birth there is very little cholesterol in the blood, but the level rises rapidly in the first few days of life. The blood level then rises slowly until it reaches adult values by the onset of puberty.

Some observers have found that there is almost invariably a fall in cholesterol levels just before or during the menstrual period. This is usually preceded or followed by a blood cholesterol level definitely above the average for each individual.

An increase in blood cholesterol is noted during pregnancy, amounting to about 25% above the average at the 30th week. This falls to the original level for the individual about 8 weeks postpartum.

The most obvious factor in the regulation of blood cholesterol levels might appear to be the dietary intake. Such is the case to a limited degree immediately following the ingestion of a fatty, cholesterol-rich meal, but the rise is both trivial (5% of ingested cholesterol) and transitory. Also a relationship between diet and blood cholesterol has been noted in individuals on strictly controlled, cholesterol-free, fat-free diets, such as the Kempner rice-fruit diet for hypertensives. On such a diet, a regular, rapid decline in blood cholesterol levels has been produced. However, moderate restriction of dietary cholesterol appears to be without significant effect on total blood cholesterol. Keys (15) studied the relationship of cholesterol levels in the diet and in the blood on 482 clinically "normal" men with diets estimated to contain from 200 to 900 mgm. of cholesterol per day. He concluded that the blood level is independent of intake over a wide range, but that at zero intake it falls at a rate related to the previous level of cholesterol in the blood. Conceivably there may be a critical intake level above zero but below 200 mgm. per day. If so, such a critical level probably differs from individual to individual. In any case, it appears doubtful that so-called "low-cholesterol" diets in current use are controlled strictly enough to reach critical levels and be of any practical value.

Another group of investigators has shown that there is a complete independency of the level of serum cholesterol and the amount of cholesterol ingested within normal dietary variations (16).

The influence of dietary fat may prove to be greater than that of dietary cholesterol in regard to blood cholesterol. Keys reports a study on one subject who was changed from a diet completely free from both cholesterol and fat to a diet containing vegetable fat but no cholesterol. The blood cholesterol of this subject rapidly increased to its previous high level on this diet devoid of any cholesterol or animal fat but containing moderate amounts of corn oil. This subject was estimated to be accumulating cholesterol at the rate of 700 mgm. daily on the latter diet (15).

Experimental hypercholesteremia in rabbits has been produced by feeding large amounts of cholesterol (17). However, the correlation of these findings with human cholesterol metabolism is questionable since the rabbit is normally a herbivorous animal. Also it has been calculated that a 143 pound man would have to eat 54 eggs a day to have a cholesterol intake comparable to those given the rabbits to produce hypercholesteremia.

There is a variety of conditions and diseases in which the cholesterol blood level is usually elevated. These include:

- Diabetes mellitus
- Anesthesia
- Nephrotic syndrome
- Jaundice
- Myxedema
- Xanthomatosis
- Acute hemorrhage
- Vitamin A deficiency
- Prolonged starvation
- Exercise
- Idiopathic familial lipemia
- Hypertrophic osteoarthritis
- Psoriasis
- Therapeutic administration of cortisone and ACTH (18)
- Atherosclerosis

The problem of atherosclerosis will be considered in detail later.

Low blood cholesterol levels are found in the following:

- Anemia
- Hepatitis
- Infection
- Hyperthyroidism
- Inanition
- Terminal states

Prostatic obstruction
Intestinal obstruction

FUNCTION OF THE LIVER IN CHOLESTEROL METABOLISM

The liver is known to excrete cholesterol in the bile and to form and excrete cholic acid. There also is evidence that the liver esterifies, synthesizes, stores, and destroys cholesterol.

Excretion—Intravenous injection of deuterium tagged cholesterol is followed by the recovery of deuterium-cholesterol in the blood, organs, feces, and bile. The liver concentration was approximately twice that of blood, while blood and bile levels were about equal. The hepatic tissue has the capacity to accumulate cholesterol and to liberate it into the blood and bile at a relatively constant and equal rate.

Formation of Cholic Acid—Deuterium tag studies (19) have shown that cholic acid is formed in the liver from cholesterol. However, administration of cholesterol will not increase the excretion of bile acids since most of the biliary cholic acid is not synthesized, but only excreted by the liver. It follows that bile acids are not of significance in the elimination of excess cholesterol.

Synthesis—Removal or destruction of large portions of the liver causes a drop in cholesterol ester blood levels. Free cholesterol remains unchanged or may be slightly lower. With healing, there is a return to normal amounts. Apparently, the deficiency of esters is directly related to the amount of liver damage, it being most severe in acute yellow atrophy of the liver. Such a relationship can be explained on the basis of impaired synthesis of cholesterol by the liver.

Storage—Ingestion of moderate to large quantities of cholesterol leads to its accumulation in the liver in the form of cholesterol esters. This is accompanied by a fall in plasma ester levels. There is also an accumulation of fat in the liver with a less than normal proportion of phospholipids.

Destruction—A rise in blood levels of cholesterol, especially free cholesterol, is noted in biliary obstruction. The failure of biliary excretion is not the primary cause for the rise since the intestinal secretion of cholesterol is elevated in states of acholia and exceeds the quantity usually excreted in the bile. Biliary excretion is not essential in maintenance of blood levels for if such were the case, biliary

cholesterol should vary with a dietary cholesterol, which it does not. One may infer, therefore, that the liver may destroy some of the excess cholesterol that enters the body.

Regulation of Free Cholesterol to Cholesterol Ester Ratio—Derangement of hepatic function causes a change in the usually constant ratio of free cholesterol to cholesterol esters, as noted above. As esters decrease in the blood, so do they increase in the liver. This inverse ratio suggests a regulatory function of the liver which may be achieved by synthesis, selection, or destruction, or the combination of all three.

Regulation of Cholesterol Esters and Phosphatides—In the liver, the fatty acids of the cholesterol esters formed in the intestine are transferred to choline phosphatides, lecithin for example. This transfer is accelerated by choline and its precursors since these substances form an essential part of the lecithin molecule. More lecithin may be made from this choline and the fatty acids liberated from the cholesterol esters. The liver may then excrete the free cholesterol in the bile. On the other hand, a choline deficiency retards such fatty acid transfer and cholesterol esters accumulate in the liver.

EXCRETION OF CHOLESTEROL

The destruction of cholesterol within the body may take place but not to a degree of consequence in the regulation of blood levels.

Small amounts of cholestanol, the hydrogenated product of cholesterol, are found in the blood stream. Small amounts of cholesterol are found in the urine.

The bile contains large amounts of cholesterol, about 500 mgm. being excreted per day, but this is not the main avenue of excretion for this substance. Bile-fistula dogs excrete amounts of sterols in the feces greater than those in the diets. Bile is, therefore, more an aid in fat absorption than in cholesterol excretion.

In the main, cholesterol excretion takes place directly into the intestine, the large bowel in particular. It has been suggested that a large portion of this cholesterol is that which is present in the leukocytes which are normally disposed of in the feces. However, free cholesterol is passed as such into the bowel also.

The fecal sterols are mainly coprosterol and dihydrocholesterol, both saturated isomers of cholesterol. Neither can be absorbed by the intestine. Coprosterol is formed in the colon since it was not isolated from contents of a ter-

minal ileostomy or cecostomy (20). It probably is a product of putrifactive bacteria.

Studies in which deuterium tagged cholestenone was fed dogs showed D_2 present in cholesterol and coprosterol (21). This substance must therefore be an intermediate product in cholesterol degradation but still with the ability to be reconverted into cholesterol. Coprostanone is always converted into coprosterol. With these facts, the chemical reactions involved in the catabolism of cholesterol are pictured as follows:

Cholesterol $\leftarrow$ cholestenone $\rightarrow$ coprostanone $\rightarrow$ coprosterol. Dihydrocholesterol is another end product of cholesterol metabolism but unrelated to coprosterol since it is excreted unaltered when fed to animals.

FUNCTIONS OF CHOLESTEROL

Although the participation of cholesterol in various reactions within the body has been proved in some instances, theorized in others, the specific function of the cholesterol molecule in these reactions is unknown.

In general, the most probable normal functions of cholesterol may be listed as follows:

1. Cholesterol aids in the absorption and transportation of fatty acids through the formation of esters, as has been explained previously.

2. Cholesterol also is known to be a precursor of cholic acid, a bile acid.

3. Vitamin D and its provitamin form in higher animals, dehydrocholesterol, are derived from cholesterol.

4. Progesterone, a female sex hormone, has been shown by isotopic studies to be composed of at least a portion of the cholesterol molecule.

5. Cholesterol may be a precursor of adrenal cortex hormone since the cholesterol content of that organ falls after administration of pituitary adrenocorticotrophic hormone (ACTH).

6. Because of such findings it is felt that cholesterol may be involved in the metabolism of other steroid hormones as well as carcinogenic steroids.

7. The large concentration of cholesterol in the white matter of the central nervous system has led to the theory that it acts as an insulating medium for the myelin sheaths of nerves.

8. It may function in the regulation of cell permeability and membrane equilibrium, those cells with a high lecithin:cholesterol ratio being more permeable to water-soluble substances.

This relationship also may effect cell growth and activity.

9. The neutralizing effect of cholesterol on venoms, bacterial toxins, bile salts, saponins, and soaps is known. The fact that the hemolytic substances, lysolecithin and lysocephalin, found in venoms are counteracted by cholesterol leads some investigators to attach significance to the almost constant cholesterol:phospholipid ratio in the body.

10. Cholesterol may be concerned with the mechanism of immunologic reactions.

Thus it is apparent that there are probably many normal functions of cholesterol in the body. A discussion of the various manifestations of dysfunction of cholesterol in the human would be in order here. But as mentioned earlier, the scope of this paper is limited, and therefore, a brief summary of the cholesterol metabolism-atherosclerosis relationship only will be presented.

ATHEROSCLEROSIS

Of prime interest today is the relationship of cholesterol metabolism to atherosclerosis. Attention has been so focused by the demonstration of the presence of cholesterol in atheromatous plaques, and by the experimental production of atherosclerosis in rabbits by feeding them cholesterol. The added fact that in certain diseases which are characterized by hypercholesterolemia, such as diabetes, there is a high incidence of premature atherosclerosis has given further impetus to the theory that cholesterol is the etiologic agent of these pathological lesions.

The presence of cholesterol in arterial atheromas is most probably due to a direct imbibition of lipids, as well as other constituents of the plasma, through the intimal endothelium under the influence of the high filtering pressure of the arteries. Atheromas contain the same lipids as plasma (22, 23). Amyloid and hyaline, as well as other colloidal macromolecular substances, can similarly penetrate into the arterial subintima.

There are two theories to explain the mechanism by which cholesterol penetrates the arterial wall. One holds that under the filtering arterial pressure cholesterol and other serum lipids enter the vessel walls in association with protein. This lipid-protein relationship has been shown to occur in the serum, and there is evidence that protein and cholesterol pass through natural

membranes together. Once within the tissues, the hydrophilic colloids, protein and lecithin, may be utilized by the cells, while the cholesterol, previously held in colloidal suspension by these substances, may be precipitated to form atheromatous plaques.

The second theory of cholesterol infiltration is based on evidence that the human blood plasma cholesterol level normally stands near the saturation point, and that cholesterol above the saturation point is precipitated. This would explain the finding of "normal" cholesterol levels in some arteriosclerotics; their serum having reached the saturation point is unable to hold more cholesterol. Precipitation may be initiated by the vibrations of the blood column. The precipitated cholesterol may be laid down on the intimal endothelium and then taken into the subintima. Some investigators believe that the solubility of cholesterol varies greatly, being progressively less soluble with advancing age.

Because of the hypercholesteremia present in animals and some humans with known atherosclerosis, investigators have been working on methods of lowering blood cholesterol levels with the view of preventing, arresting, and regressing such lesions. Attempts at lowering blood cholesterol levels have been directed at the hepatic removal of lipids with lipotropic agents, lecithin and choline, and the release of free cholesterol into the bile. However, this is of little clinical use since cholesterol excreted by the bile is reabsorbed unless the subject is on a fat-free diet.

The most vulnerable site for depleting the body of cholesterol appears to be the lumen of the bowel. Gubner and Ungerleider (12) outline the mechanisms of attack on this exogenous phase of cholesterol metabolism as follows:

- A. Decrease ingested cholesterol—this, as was shown by the work of Keys, has little or no effect on blood cholesterol.

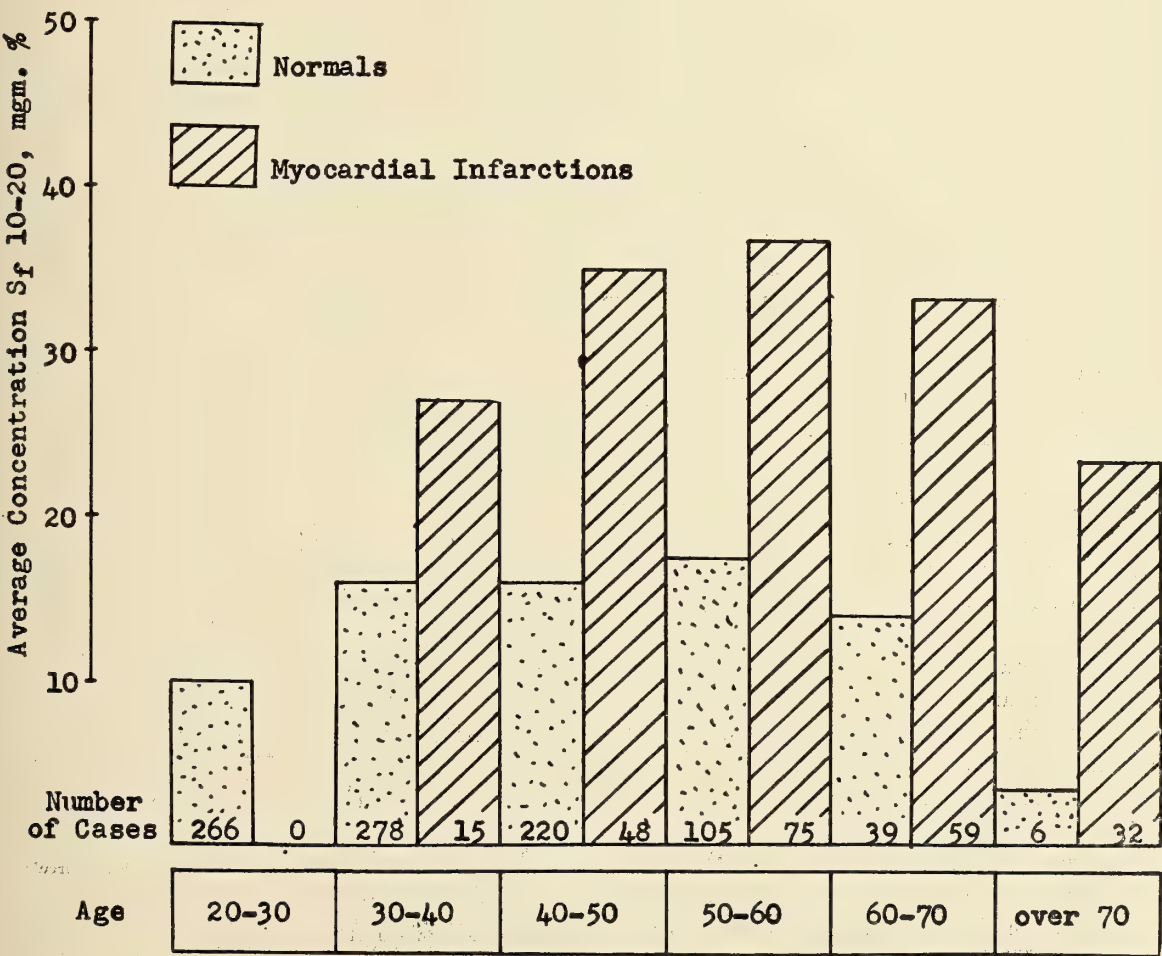


Figure V: Concentration of Sf 10-20 Molecules in Serum of Males. (24)

B. Decrease absorption of cholesterol by:

1. reducing the fat content of the diet—this reduction must be extreme to be effective;
2. exclusion of bile from the intestine—intestinal secretions also excrete cholesterol into the gut so exclusion of the bile would be only a partial measure;
3. interfering with pancreatic enzymes which are necessary for the esterification of cholesterol with fatty acids—such a condition exists in steatorrhea due to pancreatic insufficiency;
4. esterifying cholesterol with non-absorbable fatty acids, e.g., arachidic acid of peanut oil;
5. physical means which prevent cholesterol absorption—non-absorbable fat solvents, such as mineral oil, or steroid absorbing agents, such as silica gel.

C. Increase complete degradation of cholesterol in the intestines.

1. Bacterial destruction of steroids in the intestine—a diet high in meat protein favors predominance of coliform organisms which degrade cholesterol. It is possible that implantation of highly effective organisms may be an aid.
2. Chemical destruction of steroids in the intestine—selenium dioxide, cupric oxide, dinitrophenylhydrazine, and sulfite are effective *in vitro* but have not been tried *in vivo*.

Of great significance in the relationship of cholesterol to atherosclerosis is the recent work of Gofman and co-workers (24, 25). Their work indicates that ordinary chemical methods which give blood levels of free and esterified cholesterol may not be sufficiently specific to indicate the abnormal condition which occurs in atherosclerosis. They have put forth the premise that in atherosclerosis there may be a defect in metabolism of the giant serum molecules which are composed of cholesterol and its esters, phospholipids, fatty acids, and proteins and that levels of such giant molecules is of much more importance than serum cholesterol levels, *per se*.

By means of an ultracentrifuge, they have separated and identified various giant molecules on the basis of their flotation rates (expressed in Sf units). With this method they found that those molecules with a flotation rate of Sf 10-20

were apparently the ones involved in atherosclerosis production (Figure V). Furthermore, they showed that, although there is a trend toward a higher incidence of Sf 10-20 molecules as total blood cholesterol levels progress above 200 mgm%, there is no definite correlation between total blood cholesterol levels and levels of the giant molecules of Sf 10-20. Persons with cholesterol levels greatly in excess of 200 mgm% have been found with no Sf 10-20 molecules. Conversely, levels of 120-140 mgm% may have high concentrations of the giant molecules.

By placing a group of individuals on a low-fat, low-cholesterol diet (200 mgm. cholesterol and 50 gm. of fat or less per day), Gofman and associates have noted a consistent trend toward lowering the concentrations of the Sf 10-20 components in the blood regardless of the initial value. The rate of reduction varied greatly but was, none the less, conclusive.

In the light of this work, the significance of previous efforts to lower total blood cholesterol is difficult to assess at this time.

In conclusion, it may be said that we still know relatively little of the metabolism of cholesterol, perhaps one of the most important substances in the body, and that we are only on the threshold of solving the problem of its relationship to atherosclerosis. Yet every fact learned is a blow struck at the greatest single cause of death in the United States today—arteriosclerotic heart disease.

* * *

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1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

Editorial

THE TWENTIETH LEGISLATURE

The State Legislature in its recent session was the recipient of much favorable comment from various sources. The Arizona Medical Association feels that it can add its share of praise following the manner in which the program it sponsored was considered. The Association was interested in four proposed laws and was responsible for their introduction. None of them in any way pertained directly to the practice of Medicine but were for the general welfare of the public. The first measure provided for the change of commitment of patients to the State Hospital for the Insane.

The Professional Board of the State Association conducted an investigation of this situation 3 years ago, and it made a number of recommendations, which included a modification of the archaic legal procedure of committing patients which has been in force up to this time. These recommendations were presented to the State Bar Association for their consideration, but for unexplained reasons they became bogged down here, and it was only after much effort on the part of Judge Lorna Lockwood, recently elected Superior Judge of Maricopa County, and Edward "Bud" Jacobson, legal representation of the Medical Association, that the bill was resurrected and placed before the legislature. It was passed by both houses without controversy.

A second measure which was passed by both houses made provision for modification of the basic science law to apply to doctors employed by the State Hospitals, the State Board of Health, etc. Under the new law these physicians will be required to have a state license to practice medicine, but will be exempted from the basic science examination. They will be unable to indulge in the private practice of medicine, and the moment they sever their connection with the state institution their state license is automatically cancelled. It is hoped this change will expedite the procuring of capable physicians for the State Institutions.

A third measure legalized a method to obtain cadavers for the study of anatomy and other scientific means by physicians and laboratories. This was interpreted by some as a long range provision for the establishment of a State

Medical School. Our information was that it had little if any opposition in the legislature. These three bills reached Governor Pyle's desk and as this is being written it is quite certain that all will be signed.

The fourth measure was the vivisection bill. This was considered to be on a basis similar to the anatomy bill. Both are needed to promote the study of medicine from the scientific standpoint. And both measures must be legalized if Arizona is to have a medical school in the future. But, without a medical school, there are a number of physicians in the State who are anxious to carry on scientific research in private laboratories. This bill passed the House, but when it reached the Senate, The National Anti-Vivisection Society unleashed its well known ignorant and fanatical propaganda. The result was that in the last days of the Session, the bill was lost because the Senate did not have time to give it proper consideration.

Aside from the four bills that the Association promoted it was vitally interested in two other pieces of legislature. The first was HB 46. This was the part of the Reorganization Plan which set up the Department of Health, Welfare and Correction. The opposition of the medical profession to proposed reorganization plans of government stems back to the national level, when the present administration in Washington attempted to set up a Department of Welfare with the Hon. Oscar R. Ewing at the head of it, with cabinet rank. The plan was turned back twice last year and the doctors of the nation were given full credit for its defeat. For a number of years the American Medical Association has been asking for a Department of Health in the President's Cabinet and the Secretary of this department to be a medical man. The present bill placed the State Department of Health under the Commissioner of Health, Welfare and Correction, and further stated that the Director of Public Health would be a political appointee who could be removed without cause. The Association disapproved of this feature of the bill and gave public notice of its action. But it was found that both Houses of the Legislature and the Governor had their minds set on the enactment of this reorganization plan. The information was passed along that Dr. Clarence G. Salsbury, at present employed in the State Department of Health would

be named Commissioner of the State Department of Health, Welfare and Correction. The bill was passed and has become law. The State Medical Association has full confidence in the integrity and ability of Governor Pyle and Dr. Clarence G. Salsbury. For many years Dr. Salsbury was Medical Director of the Ganado Indian Hospital in Northern Arizona and is well known to the doctors of the state. But the Association is concerned over Governors and Commissioners of the future.

The legislature turned thumbs down on the proposed Naturopathic Bill. The Superior Court has ruled that naturopaths cannot prescribe, and this decision has been appealed to the State Supreme Court. This bill, would have legislated the naturopaths of the State into full fledged prescribers of drugs, under the pretense of allowing them to prescribe nutritional substances. The legislators realized as well as all others that the naturopaths would be either prevented or allowed to prescribe by statute, and if allowed to prescribe nutritional substances, there would be no limit to what such a broad term would include. In other words, the only way to limit their prescribing, would be to prevent all prescribing. The bill did not emerge from Committee.

So again the Arizona Medical Association wishes to commend Governor Howard Pyle and the Twentieth Legislature for the harmonious methods they pursued in attempting to legislate for the common welfare of the public as well as for the majority.

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PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL HOSPITAL CASE NO. 29071

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A sixty-five-year old woman entered the hospital because of "gas around the heart" and palpitation.

Approximately one year before entry the patient developed slight constipation, which was relieved readily with mineral oil or milk of magnesia. Since that time she had had intermittent attacks, that is, two or three times per month, of periumbilical crampy pain, each lasting several hours. These were unrelated to food intake or activity and were sufficiently severe on only one occasion to force her to bed. She had had no recurrence of this pain during the four or five weeks prior to admission. She attributed this to pills prescribed by her physician. However, five weeks before entry she began to suffer with considerable belching and sour eructations. The belching was worse at night and half an hour after meals, but was otherwise not related to activity and was not effected by bowel movements. During this same period, palpitation frequently occurred at night. At no time had there been malaise, anorexia, nausea, vomiting, diarrhea, melena, jaundice, dyspnea, orthopnea or ankle edema.

The family and past histories were non-contributory.

Physical examination revealed a moderately obese, somewhat apprehensive woman who did not appear to be uncomfortable. The chest was barrel shaped. Examination of the lungs was negative. The heart was considered enlarged to the left; the sounds were of good quality and no murmurs were audible. The abdomen was soft. There was slight tenderness and a poorly defined mass in the left lower quadrant.

The blood pressure was 167 systolic, 90 diastolic. The temperature was 97.6°F., the pulse 88, and the respirations 18.

The examination of the blood revealed a

hemoglobin of 14.7 gm. and a white-cell count of 9700 with 69 per cent polymorphonuclear leukocytes. The urine was normal except for a rare white and epithelial cell in the sediment. A gastric analysis revealed no free acid in the first specimen and 15 units in the specimen collected an hour later. The gastric contents were guaiac negative. Repeated stool examinations were guaiac negative. A Graham test was negative. A barium enema showed narrowing and marked mucosal swelling of the mid-portion of the sigmoid over a distance of approximately 10 cm. Definite ulceration of the mucosa was not visible. There were numerous diverticula in the sigmoid and descending colon. The colon proximal to the lesion was not examined. Ten days later the barium studies were repeated, barium being introduced by means of a Foley catheter. At this examination there was complete obstruction in the sigmoid in the area of greatest narrowing previously described. The exact nature of the lesion could not be demonstrated because insufficient barium passed the point of obstruction.

An operation was performed on the sixteenth hospital day.

DR PALMER DYSART

Since my fellow discussants have or will plagiarize and draw freely on my comprehensive and classical epic in medical literature on constricting lesions of the colon, published in a recent issue of Arizona Medicine, I will not have to devote much time to further discussion of the basic factors involved in the diagnosis of such a lesion as we are presented with in this case.

Non-malignant strictures of the colon are rare except in connection with diverticulitis, according to Dysart et al. With this lesion occurring in the left colon, the possibility of the constriction being due to a specific type of infection, such as tuberculosis either hyperplastic or ulcerative, and regional or segmental ileo-colitis, becomes more remote. Of course ulcerative colitis is more common to the left of Cannon's ring in the transverse colon, but constriction is not the outstanding feature of this condition.

Of malignant tumors of the colon, sarcoma is the most rare and involves the proximal half of the colon nearly exclusively. Sarcoma characteristically involves an extended portion of the wall of the intestine to produce a tube-like

constriction without mucosal ulceration which could fit the description of the findings in this case upon barium enema, which were described as narrowing and marked mucosal swelling of the mid-portion of the sigmoid over a distance of approximately 10 cm. without definite evidence of ulceration of the mucosa. Numerous diverticula were found in the sigmoid and descending colon.

Carcinoma of the sigmoid colon is much more common than sarcoma. While carcinoma of the right half of the colon is usually fungating, it is more often of the scirrhous type in the left half, but this does not tend to simulate the extensive tube-like invasion of sarcoma, but is more localized.

We are presented with several interesting facts some of which are in apparent conflict. This patient is a 65 year old moderately obese woman who, because of constipation and increasing gastro-intestinal symptoms for a year, is found to have a progressive constricting lesion of the sigmoid colon over a distance of 10 cm. without ulceration. Coincidentally, or possibly associated with this, a diverticulosis of the descending and sigmoid colon was found.

With a known diverticulosis, and a constricting lesion, a diverticulitis is immediately suggested. But, the single reported temperature recording of 97.6 degrees does not indicate much sepsis, and most important of all, I would expect blood to be present in the stools in acute diverticulitis. A white cell count of 9700 with a differential count of 69% polymorphonuclear leucocytes is equivocal. A hemoglobin of 14.7 gm., the obesity and the absence of blood in the stools, do not suggest far advanced malignancy of the colon, nor rule it out, for the systemic effect of carcinoma of the left colon is a late manifestation.

Neoplasm, usually listed as a sequel of diverticulitis is, according to Walter Palmer, probably merely a coincidence. This can well be so, for with an overall incidence of cancer in the total population at some time during life placed currently approximately at 20%, and a general incidence of 2% of all deaths listed as being due to gastro-intestinal cancer of which 40% occurred in the colon, the incidence of diverticulosis in adults was found at the Mayo Clinic to be about 5%. It would therefore be difficult to prove more than coincidence in the presence

of carcinoma of the colon where diverticulosis exists.

Coincidence or the result of diverticulitis, carcinoma does occur associated with diverticulosis, and I believe that because of the absence of evidence of an acute infectious process which should accompany a progressive constriction of the sigmoid due to a diverticulitis, this is a case of scirrhous carcinoma of the sigmoid associated with diverticulosis.

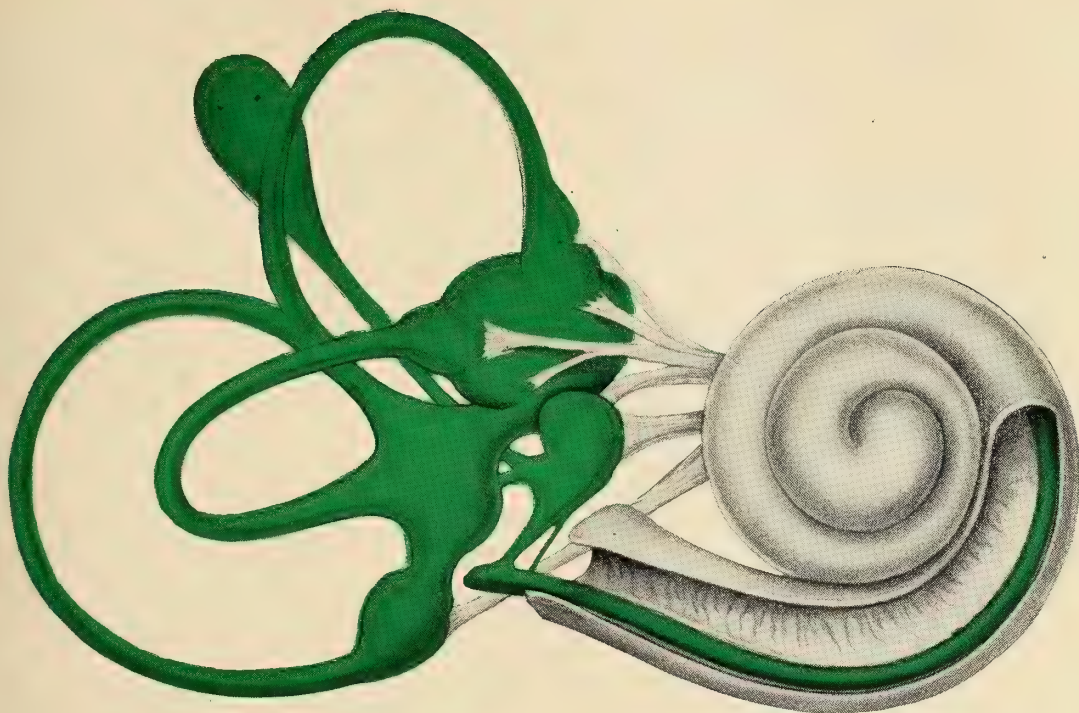
DIFFERENTIAL DIAGNOSIS

Dr. Reginald M. Smithwick: The history indicates that this sixty-five-year-old woman had had symptoms referable to the gastrointestinal tract for about a year. One of these was slight constipation, which apparently did not increase in severity and was easily relieved by nondrastic laxatives. There were also short periods of crampy abdominal pain occasionally lasting several hours. Later, belching and sour eructations but no nausea or vomiting were noted. There was no distention, increased peristalsis or fever. An indefinite, slightly tender mass in the left lower quadrant tends to incriminate the large intestine. This was confirmed by a barium enema, which revealed a process involving the midportion of the sigmoid—with marked narrowing on the first examination and complete obstruction on a second examination ten days later. There is no evidence in the history of other clinical signs of complete obstruction, such as distention, pain, increased peristalsis, nausea and vomiting. Apparently her bowels moved in spite of the x-ray evidence of marked obstruction, since it is reported that repeated stool examinations were negative for occult blood.

The question for discussion seems to be the nature of the lesion in the sigmoid colon. The x-ray suggests an intrinsic process. A review of the films may be helpful.

Dr. George W. Holmes: There is nothing of interest in the chest. The gallbladder is well seen and looks normal. The colon is obviously abnormal, and the picture is characteristic of diverticulosis, with multiple large diverticula scattered throughout the descending colon and sigmoid.

At one examination there was no definite obstruction. At another examination ten days later there was definite obstruction. At first examination, in addition to the diverticula,



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—Tuttle, A. D.: *Special Breakdown of Case Histories*, presented at the Airlines Medical Directors Association Meeting, New York, N. Y., Aug. 28, 1949.

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there was evidence of spasm. The film taken in the lateral view shows a good outline of the lumen of the large bowel, and it does not seem possible that a tumor large enough to plug the bowel could have been present and have been completely missed at this first examination. At the second examination the filling is insufficient and one could miss a tumor, but I should not expect a large tumor to appear in such a short interval. So far as the x-ray demonstration goes there was no ulcerated lesion or tumor, so our interpretation would be that the obstruction was due to the diverticulitis.

Dr. Smithwick: The two most likely diagnoses are carcinoma and diverticulitis, with or without a localized perforation and abscess. It is possible that both lesions were present. These seem more probable explanations for the sigmoid lesion than tuberculosis, lymphoma, endometriosis, metastatic carcinoma or the extension of a primary lesion of the left uterine adnexa to the bowel. There is no evidence of a benign polypoid tumor of the bowel.

With regard to the differential diagnosis between cancer and diverticulitis, it is at times easy, at times difficult, and occasionally impossible. The age of the patient is not helpful, since either lesion is probable at sixty-five; and the duration of symptoms is quite in keeping with either diagnosis. The absence of clinical symptoms of increasing constipation favors a diagnosis diverticulitis, whereas the x-ray evidence of complete obstruction leads one to favor cancer, particularly if it persisted after a few weeks of proximal decompression of the bowel. The location of the lesion—the sigmoid area—is a characteristic one for both carcinoma and diverticulitis. The absence of blood in the stools is definitely in favor of diverticulitis, since bleeding is present in only about 16 per cent of the cases of diverticulitis and usually occurs in cases of cancer. The presence of a mass is not helpful. Even at operation one often cannot differentiate the two lesions by inspection or palpation. The pathologist has to decide the matter following resection of the involved area. The x-ray evidence obtained from the first barium enema favors diverticulitis because of the long segment involved (10 cm.) and the absence of destruction of the mucosa. The presence of both lesions is statistically unlikely, as diverticulums have been found associated with carcinoma in only 0.6 per cent of cases, whereas

cancer has been found associated with diverticulitis in only 1.8 per cent of cases.

It seems to me that the evidence at hand favors a diagnosis of diverticulitis of the sigmoid with a recent increase in the inflammatory process; an associated localized perforation is a reasonable explanation for the recent x-ray evidence of complete obstruction.

Dr. Tracy B. Mallory: If you had a choice between the two alternatives, Dr. Holmes, which would you choose from the x-ray point of view?

Dr. Holmes: There is no x-ray evidence of tumor. If we made the diagnosis from the x-ray examination alone we should have to say diverticulitis.

CLINICAL DIAGNOSIS

Diverticulitis.

DR. SMITHWICK'S DIAGNOSIS

Diverticulitis of sigmoid.

ANATOMICAL DIAGNOSIS

Carcinoma of sigmoid.

Diverticulosis.

PATHOLOGICAL DISCUSSION

Dr. Mallory: This patient was operated on and a segment of the sigmoid was found to contain many large and deep diverticulums. The involved segment was moderately firm. The surgeon's preoperative diagnosis was diverticulitis. When he finished the operation he apparently wavered a bit, since he raised the question of carcinoma; but he still put down diverticulitis as his first diagnosis.

When the sigmoid was opened in the laboratory, a small annular cancer was found in the midst of the segment, which had caused a significant grade of obstruction. We could find no evidence that any of the diverticulums were inflamed, and we thought that they were purely coincidental and that the symptoms were due to carcinoma.

Dr. Smithwick: How do you explain the difference in the barium enema in ten days?

Dr. Mallory: There might have been enough difference in the pressures used during the two examinations.

Dr. Holmes: So one got through and the other did not? I hardly think so. Where was the cancer?

Dr. Mallory: In the midst of the area of diverticulosis in the sigmoid.

Dr. Holmes: At the second examination the obstruction does not seem to be abrupt, and I wonder if they failed to get the enema in.

TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER, M.D.

Important conclusions on **DRUG THERAPY FOR TUBERCULOSIS** were reported at the Atlanta meeting of the **'TENTH STREPTOMYCIN CONFERENCE** of the Veterans Administration and the Nat'l. TB. Ass'n., January 25th to 28th,—

1. The best clinical effect, with a scanty bacterial resistance, is obtained from **ONE GRAM** of streptomycin **TWICE A WEEK**, accompanied by 12 grams of PAS daily.

2. Daily PAS seems more helpful than bi-weekly.

3. The use of large versus small doses, and daily versus biweekly doses of streptomycin for **ACUTE LESIONS** is still controversial. All seem to work.

4. The comparison of streptomycin and dihydrostreptomycin has not produced a final answer. In the current dosage schedule there is scanty difference.

5. Chemotherapy may seal off secretions and caseations. Bacilli may become 'quiescent'. The 'necrosis factor' may determine relapses when drugs are discontinued.

6. Prolonged therapy may have an added value, with 4 months a minimum, and 6 to 12 months being possibilities in certain cases.

7. Chemotherapy may be added to collapse therapy with profit.

8. Cortisone and ACTH must be considered hazardous.

9. Viomycin, mycomycin, neomycin, etc. are still too toxic for use in humans.

We have at hand eleven articles on CIVIL DEFENSE and/ or THE ATOM BOMB. All of them describe general conduct, and give a list of the types of injury from the bomb. Sixty per cent of those affected will have flash or flame **BURNS**, yet not a single one of these outlines gives the best immediate treatment of a burn. . . . We will bend an effort to find out what is the best initial therapy, and publish it here.

Freeman and Young of Temple, Texas, report again on **SKIN DISINFECTION**. They studied 1,131 operative incisions made during one calendar year (Archives of Surgery, November, 1950). . . . A detergent (phisoderm) and a new antiseptic (3% hexachlorophene) were used on the surgeon's hand and the patient's skin. A 2-minute scrub with these preparations is as good as a 10-minute scrub with soap, they say.

The investigative group at the University of Arizona and The SOUTHWESTERN CLINIC

AND RESEARCH INSTITUTE, Tucson, has reported a piece of work in the Proc. Soc. Exper. Biol. and Med. . . . ACTH and cortisone increase the output of certain amino-acids. Each affects threomine and tyrosine; ACTH increases lysine; neither affects argenine.

The report on the use of **PRISCOLINE** in **POLIOMYLITIS** in Brooklyn (847) patients) is worth emphasizing. . . . The quick action, relief of pain, recession of muscle tightness and spasm, improved skin temperature were notable. The reduction in the 'service' requirements was most important, tho, since hot packs were not needed and transfer of patients occurred earlier. . . . Reports from the recent season should serve to evaluate the usage.

The effectiveness of 'Tapeway', an ADHESIVE-TAPE REMOVER, is good. . . . It has an odor faintly like acetone; does not inflame the skin (like benzine); does not evaporate, nor repel the patient, as does ether. . . . It works poorly on waterproof tape. It quickly cleans the crumbly and adherent residue left by tape. . . . Olson of Wisconsin has demonstrated that the liquid does not irritate incisions, even in excess, and actually is antiseptic.

Two **PHONE-ANSWERING DEVICES** have recently been described in 'Medical Economics'. The Electronic Secretary sells for \$250 to \$426, and the Tele-Magnet costs \$299.50.

INHALATION OF HUMAN THROMBIN is said by Wassersug to control pulmonary hemorrhage, whether due to tuberculosis, neoplasm, bronchiectasis, et al. (Dis. of Chest). Only a few cases have been reported. They were given 1 or 2 cc. of a saline solution containing 500 to 1000 units of thrombin per cc. . . . Human thrombin is preferred to the ordinary bovine thrombin because it lacks the allergic effect of the latter. . . . If this method works out well, we can use it in addition to the recently reported intravenous pituitrin—provided pituitrin works out well.

Hope, in an old guise, has appeared again for **MULTIPLE SCLEROSIS** patients. . . . Jonez has reported in the Annals of Allergy the favorable effects of **HISTAMINE** in 152 cases—a large series in any league. Both acute and chronic cases seemed to benefit. . . . The drug has been used before (1940-45), but has seemed to be just another

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method in most hands. The current approaches were intravenous, subcutaneous, and iontophoresis. . . . Iontophoresis is easiest for home or office use, but must be preceded by at least 30 intravenous injections.

Irvin and Burgess have reported in the *New England Journal of Medicine* that **PROLONGED REST** after **MYOCARDIAL INFARCTION** is **NOT** desirable. It may be physically and mentally harmful. . . . They believe that two weeks of bedrest, with bedside toilet privileges, is enough in most cases. Walking is then begun, and the patient may leave the hospital in about four weeks. The regimen may be modified to fit circumstances. . . . A sitting position and some movement avoid the hazards of atelectasis, pneumonia, phlebothrombosis, angina pectoris, etc. Psychogenic sequelae are minimized. . . . Arrhythmias and rupture are usually restricted to the first 2 weeks.

Dr. Joseph Aronson of the Phipps Institute of Philadelphia is the person who has most carefully studied the tuberculin sensitivity, and the value of B.C.G. VACCINE, among the American Indians. . . . He has recently (in the *American Review of Tuberculosis* for February 1951) summarized the fluctuation of tuberculin reactions among the various tribes, living in various geographical areas, as observed during a period of 9 to 11 years. . . . **ARIZONA CLIMATE**, containing sunshine and perhaps some other elusive factor, is given a huge boost, as follows,—“Fluctuation of the tuberculin reaction, as well as reversions from positive to negative, occurred most frequently among the controls and BCG-vaccinated persons living at the Pima Agency, Arizona. The instability of the tuberculin reaction noted among the BCG-vaccinated living at the Pima Agency, Arizona, cannot be attributed to the low antigenicity of the

BCG vaccine, but possibly related to climate factors such as excessive sunlight.”

The status of **PREGNANCY AND TUBERCULOSIS** has become fairly well resolved. A dozen years ago the clinicians at the Sea View Hospital in New York suggested the heretical idea that the two conditions may coexist without special detriment to the mother. . . . Early pregnancy offers no contradiction to surgical or medical treatment of tuberculosis, and the mortality rate is about the same as for the non-pregnant. . . . Proper management and individualization of the pregnancy produces no special hazard to a controlled TB. Delivery is given special care, and the weeks pre and post-partum are carefully protected, and with special freedom from strain. . . . The mother and child are separated for a time after birth, and the infant should be vaccinated with B.C.G.

A letter from Dr. Sol Rosenthal, head of the Tice BCG Laboratory at Cook County Hospital, says that **THE NEW DRIED BCG VACCINE** has reached the stage where it is now in the hands of the Washington authorities. . . . The disadvantage of the present vaccine is the need to use the suspension within a week, and to be refrigerated or in thermos during shipping and until used. . . . The new material is viable for many months, may be shipped thru the mails without insulation, and produces a high percentage of ‘takes’ by multiple puncture vaccination. . . . Tice Laboratory was the first one licensed for interstate commerce, in 1950.

A physician of three hundred years ago, Sir Thomas Browne, gives us some comforting reassurance in his ‘*Religio Medici*’,—“**THAT GENERAL OPINION THAT THE WORLD GROWS NEAR ITS END HATH POSSESSED ALL AGES PAST AS NEARLY AS OURS.**”

“A NEW MILESTONE IN PREPAID MEDICAL CARE”

An Address By

ELMER L. HENDERSON, M.D.

President, American Medical Association

Delivered Before The

**UNITED MEDICAL SERVICE OF
NEW YORK**

*At a dinner meeting held in observance of the
United Medical Service's enrollment of its
2,000,000th member*

January 25, 1951

Hotel Biltmore, New York City

I am honored to have the opportunity of being with you here this evening on this significant occasion. And I am extremely happy to add my tribute, and that of the American Medical Association, to the United Medical Service for having

enrolled its two-millionth member in the Metropolitan New York area.

This achievement is of both local and National significance. It not only demonstrates the great progress being made by all types of Voluntary Health Insurance in the New York area; it also is representative of the rapid growth and development, and the promising potentialities, of all the Voluntary Health Insurance Plans throughout the entire Nation.

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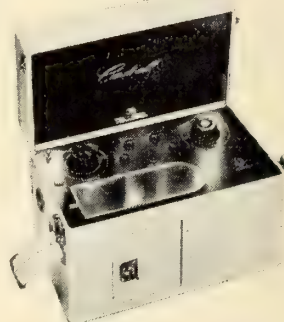
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of the Medical Society of the State of New York, and of the medical societies in those seventeen counties—the United Medical Service has shown a vigorous, progressive development during its six and one-half years of existence.

Your organization, by virtue of both its experience and its excellent leadership, also has contributed much to the National evolution and improvement of Voluntary Health Insurance. It is noteworthy that three of your top officials also are members of the National board known as the Blue Shield Commission: your President, Dr. Charles Gordon Heyd—who is a Past President of the American Medical Association—and Mr. John F. McCormack and Dr. Frederick Elliott.

At the moment, according to my latest information, the United Medical Service is the second largest of the non-profit plans providing insurance protection against surgical and medical bills. I understand that the Blue Shield plan in Michigan, the Michigan Medical Service, edged slightly ahead of you just two or three months ago.

However, I also understand that the United Medical Service of New York is determined to regain first place, and to hold it permanently. Regardless of which particular plan is the largest or the best, it is that spirit of competition which assures that sound, low-cost protection soon will be available to every American who needs and wants Voluntary Health Insurance.

The United Medical Service, I am told, aims at a total enrollment of three million persons within the next year or year and a half. Knowing what you accomplished in 1950—when you gained half a million new members, or one-fourth of your present total enrollment—I am confident that you can and will reach your goal.

My confidence extends to all groups in the Voluntary Health Insurance field—the Blue Cross hospital plans, the Blue Shield medical care plans, all the other non-profit plans sponsored by hospitals and physicians, the insurance companies, and the many plans sponsored by labor unions, fraternal organizations, business and industrial concerns, and other sound agencies. Among all of them, whether they are operating in cooperation or in competition, there is a determination to prove that voluntary methods are the best answer to our medical care problems. And *from* all of them there are continuous

reports of rapid growth, improved coverage and new developments.

For example, the Nation's Blue Shield plans alone gained five million new members during 1950, for a new record year of growth. The increase last year exceeded the previous high gain in 1949 by almost two million.

The Blue Shield plans are enrolling new members at the rate of 28,000 every working day, and they now protect more than seventeen million persons, or approximately twelve per cent of the population. Other non-profit medical care plans, which are not yet in the Blue Shield group, cover an additional two and one-quarter million people, making a total of nearly twenty million in just the physician-sponsored plans alone.

There now are seventy-two Blue Shield plans in forty-one States, and participating in their operations are 113,000 out of the 150,000 physicians who are in active, private practice. Last year the Blue Shield plans paid out \$150 million for surgical and medical services rendered to member patients.

The Blue Cross hospital plans added more than three million new members in 1950, and they now are beyond the forty million mark in total enrollment.

Out of every dollars paid in premiums, the Blue Shield plans now are paying out eighty-two cents in benefits, and the Blue Cross plans are paying out close to eighty-six cents in benefits.

The facts and figures I have been citing relate mainly to the Blue Cross and Blue Shield plans. The same kind of progress was being made during 1950 by the insurance companies and the various other agencies in the health insurance field, but complete, final figures from all those sources will not be available for several months.

At the end of 1949, we know from the last annual report of the Health Insurance Council, more than sixty-six million Americans had some kind of voluntary insurance protecting them against hospital, surgical or medical expenses. It is a conservative estimate, based on all known developments in 1950, that between seventy and seventy-two million Americans now have some form of Voluntary Health Insurance.

The Voluntary Health Insurance Plans not only are growing rapidly, but they also are developing new and improved types of coverage,

based on sound actuarial standards. As a result of the so-called catastrophic coverage pioneered early last year by the California Physicians Service, fifteen of the Blue Shield plans now are preparing to offer protection against the prolonged, costly illnesses such as heart disease, cancer and others. A number of insurance companies also are experimenting with this type of coverage, or are planning to introduce it in the near future. All of the non-profit plans, the insurance companies and other agencies in the field are studying this important development.

Market progress also is being made in making individual coverage more widely available for persons who cannot get group health insurance. Practically all of the Blue Shield plans, and many of the insurance companies, now offer individual enrollments. Maximum progress in this direction is one of the vital objectives of the medical profession and all others interested in the continued growth of Voluntary Health Insurance.

Another problem which is receiving serious, intensive study, and which ultimately must and will be solved, is how to extend Voluntary Health Insurance protection to older persons who are beyond the retirement age.

The remarkable growth and development of Voluntary Health Insurance—which has taken place mainly in just the past ten years, and which still is gaining momentum—is proving that voluntary methods can take the economic shock out of illness, and that dangerous Government intrusion in the field of medical care is completely unnecessary.

The prediction of medical economists—that ninety million Americans will be protected by Voluntary Health Insurance within the next two or three years—is well on its way to fulfillment . . . and the advocates of socialized medicine are fast losing all semblance of a case.

Voluntary methods also are demonstrating their worth and vitality in the solution of other problems involving the supply and distribution of medical service. Throughout the Nation, many State and County Medical Societies are conducting highly successful programs for placing doctors in communities which need them, for providing medical facilities where needed, for supplying 24-hour emergency medical service, for settling the complaints of patients, for informing the public on matters pertaining to

health and medical care, and for insuring adequate medical service for all who need it.

Such programs are proving that effective action can result from close cooperation among doctors, medical schools, public officials and the people of the community. The American Medical Association is urging and promoting the fullest possible development of such programs in every State, County and locality in the country. This is just one more part of the American answer to those who would socialize medicine first, and the rest of the Nation soon after.

There is still another area in which we must prove conclusively that American, voluntary methods can do the job. This is the problem of financial aid to medical education—a matter which has been aggravated and given added prominence by the present National emergency, and also by a great deal of distorted, inaccurate propaganda.

The Board of Trustees of the American Medical Association, at the clinical session last month in Cleveland, took the lead by appropriating half a million dollars as the nucleus of a fund to be raised for the aid of medical schools throughout the Nation. Pointing to the dangers of Federal interference in medical education, the A.M.A. Board of Trustees said: (and I quote)

"There is a growing public awareness that Federal subsidy has come to be a burden, not a bounty, for it is bringing intolerable increases in taxation, and is dangerously increasing Federal controls over our institutions and the lives of our people." (end of quote)

The board expressed the hope that its action will stimulate other professions, industries, businesses, labor groups and private donors to help swell the fund for medical education—and it urged all American doctors to contribute individually, and to take the lead in obtaining contributions from other sources.

Since that time there has been a heartening response, in the form of contributions, pledges and expressions of approval and encouragement, from many individuals and organizations both in and out of the medical profession.

As the second concrete step in this project, the American Medical Education Foundation, a non-profit corporation for the receipt of funds for medical education, has been organized under the laws of Illinois. Contributions to the Foundation can be addressed to 535 North Dearborn Street, Chicago 10, Illinois.

The American Medical Association intends to give this drive for funds the widest possible publicity in all medical publications and newsletters reaching doctors. I urge everyone present here tonight, whether doctor or layman, to do everything he possibly can to contribute individually, to encourage donations by others, and to cooperate in any future fund-raising plans which may be announced.

Assuring an adequate future supply of doc-

tors—through American methods which will preserve the standards and freedom of medical education—is of vital importance to the continued success of the medical care plans, to all those engaged in the provision of health services, and to every American citizen. The medical profession is willing to take the lead, but it also needs and asks the help of all Americans who prefer initiative and enterprise to Government domination and control.

REPORT OF THE ARIZONA ADVISORY COMMITTEE TO SELECTIVE SERVICE SYSTEM

The Council of The Arizona Medical Association, Inc., at a meeting held January 25, 1951, indicated its desire that a report of this Committee be made periodically to the members of the Association in order that they may be informed of our activities.

To those of you who might not have knowledge of our organization and operation, and without going into too much detail, I might say that its Chairman was appointed by the Chairman of the National Advisory Committee to the Selective Service System, Dr. Howard A. Rusk, as his medical representative for the State of Arizona. Dr. William A. Baker was likewise appointed to represent the dental profession of the State, and Dr. James P. Ward the Public Health interests. Your representative immediately thereafter appointed the membership of the Procurement and Assignment Committee of the Medical Association to assist. As some of you may know, this Committee membership is composed of Drs. Francis M. Findlay, Robert E. Hastings (President), Hilary D. Ketcherside, Harold W. Kohl, Jesse B. Littlefield, Robert M. Matts, Joseph P. McNally, Frank J. Milloy (Secretary), and myself as its Chairman. I likewise appointed Dr. R. J. Hight, State Veterinarian, representing the veterinary profession. The purpose of the Arizona Advisory Committee is to assist the National Committee in an advisory capacity to the Selective Service System in the mobilization of the medical, dental, and veterinarian manpower. So much for organization.

On January 12 and 13, 1951, at the call of the National Chairman, Dr. Rusk, a meeting was held in Washington, D. C., attended by your Chairman, Dr. Baker, Dr. Ward, and Robert Carpenter, Executive Secretary of the Association. This meeting was to acquaint the local

State Advisory Committees on operational procedures and the major problems which lie ahead. I will not go into detail on the discussions which took place, as I have already appeared before the Pima County Medical Society the early part of last month and made a full report; also a representative group of the Maricopa County Medical Society. I might add, however, that we were all impressed with the urgency of the situation and the major role that the medical, dental and veterinary professions will be called upon to play in this national emergency.

You are all aware of the military questionnaire sent out many months ago requesting certain information necessary to assist the Committee in its deliberations. Recently, and at the request of the National Advisory Committee, a second questionnaire, briefed and in the form of a card, has been mailed to each physician in this state in order to bring the record to date and for uniformity nationally, and the response has been gratifying. I wish to take this opportunity to thank you for your participation as your cooperation is essential to the effectiveness of our work.

On January 31, 1951, there was issued from the State Headquarters of the Selective Service System a report tabulating those registered in the three professions with Selective Service in Priorities I and II, also III and IV. You will be interested to know that there have been registered up to that date 28 medical doctors in Priority I, 9 in II, 149 in III, and 205 in IV.

Following receipt of this report and study of the results of the Local Boards' individual classifications, a meeting was requested and granted by the State Director of the Selective Service System, and recently your Committee met, primarily for the purpose of better under-

standing the local procedures and operations in order that the Advisory Committee may assume its full responsibility and coordinate its activities with those of the State Director; also to review the results of the individual classifications, especially as pertains to those deferred. While to date there has been limited activity on the part of our Committee as pertains to the group in Priorities I and II, our first real problem will present itself just as soon as Priority III, and thereafter Priority IV, is reached. At the present moment it is expected the calendar will be maintained; i.e., that all of Priorities I and II will be called to service within the next four to six months, and unless the international picture changes appreciably by the end of the year the call for Priority III will have been reached. Effective April 1, 1951, and thereafter, all Reserve Officers will be screened by our Committee in

accordance with previous order. Your Committee is giving very close attention to the screening process, and as stated before, especially to those individuals receiving temporary deferment. There is no such thing as permanent deferment, and every case of temporary deferment will be reviewed, particularly with the objective to assure replacement wherever possible in order that those so temporarily deferred may be relieved for military duty at the earliest possible moment.

Complete understanding and a united spirit of cooperation is evinced between the office of the State Selective Service System and your Advisory Committee, and every effort will be made to achieve an orderly withdrawal of medical, dental and veterinary doctors to meet both the military and civilian needs.

Joseph M. Greer, M.D., Chairman

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SECRETARY LULL'S LETTER

"The Key to Peace"—An American Classic. The physician who can find a few spare moments should read Clarence Manion's American classic, "The Key to Peace."

The American Legion was so impressed by the quality and the importance of Mr. Manion's dynamic and thrilling restatement of American principles that it is giving the 120-page book widespread distribution.

Copies have been sent to all members of the A.M.A. Board of Trustees and of the Campaign Coordinating Committee. President-Elect John W. Cline, San Francisco, was so impressed after reading it that he sent the publishers, The Heritage Foundation, Inc., 75 East Wacker Drive, Chicago 1, a letter in which he said he sincerely hoped that "it would be read by every physician in the country."

"I have read and reread 'The Key to Peace'," Dr. Cline said in a letter to Dean Manion, who heads the College of Law of Notre Dame University. "It is one of the most penetrating treatises on American political thought I have encountered and is an extremely important contribution. I sincerely hope that it will have wide-spread circulation and know that it cannot fail to impress upon people the necessity of preserving individual freedom in this country."

Many who have read the book say that it is the best statement of the philosophy of freedom ever written.

Here are a few excerpts:

"It is to the private enterprise of American men and women that an enslaved and starving world looks today for food and sustenance. If state-owned and state-controlled economies could outproduce private enterprise uncounted millions of men and women would not have died of starvation in Soviet Russia since 1920. Neither would we now be considering the indefinite extension of the 'Marshall plan' every dollar of all of which is in addition to the more than 50 billion dollars worth of goods that we have donated to foreign governments since the end of World War II."

—o—

"Here is one example of centralized governmental operation: Paul wants some of Peter's property. For moral as well as legal reasons, Paul is unable personally to accomplish this desire. Paul therefore persuades the government

to tax Peter in order to provide funds with which the government pays Paul a "subsidy." Paul now has what he wanted. His conscience is clear and he has proceeded 'according to law.' Who could ask for more?—why, Paul, of course, and at the very next opportunity. There is nothing to stop him now except the eventual exhaustion of Peter's resources."

—o—

"It has been correctly stated that socialism is communism on a slow train. Socialism performs its totalitarian operations under the anesthetic of 'democratic' terminology while communism draws the same blood visibly, violently and with an open profession of its complete and unrestrained dictatorship."

—o—

"In 1936, Mr. John Strachey wrote in his 'Theory and Practice of Socialism': 'It is impossible to establish communism as the immediate successor to capitalism. It is, accordingly, proposed to establish socialism as something which we can put in the place of our present decaying capitalism. Hence, communists work for the establishment of socialism as a necessary transition stage on the road to communism.'

"At this writing, Mr. Strachey is War Minister in the Socialist government of Great Britain."

—o—

"The process of governmental liberation takes different forms at different times. In recent years the process has taken the form of taxing and spending by the federal government. The successful use of this form of governmental liberation constitutes the most serious threat ever made against the maintenance of constitutional limitations in the United States."

—o—

"Unless constitutional limitations upon the spending powers of Congress are effectively and speedily established, all other constitutional limitations will soon be swept aside in our constantly accelerated drive toward centralized socialism. Money is power and, when the materialistic concept controls, unlimited money is unlimited power."

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"Today, big and complicated government has a hand in everybody's business and another in every person's pocket. These hands are moved by relatively obscure people tucked away here and there throughout the fathomless maze of government's bulging bureaucracy."



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Dr. Philippe Bauwens (Chairman of the Executive Committee).

Hon. Secretary: Dr. A. C. Boyle.

Address: 45, Lincoln's Inn Fields, London, W.C.2.

The Congress will be held in London from the 14th to the 19th, July, 1952.

In accordance with the regulations of the International Federation of Physical Medicine, the meetings of the Congress will be reserved for matters dealing with the clinical, remedial, prophylactic and educational aspects of Physical Medicine and with the diagnostic and therapeutic methods employed in Physical Medicine and Rehabilitation.

Technical, scientific and historical Exhibitions also will be arranged.

In addition to the Scientific Program, a full programme of social events and entertainment is being planned for the members and associate members. Arrangements for London and provincial visits of scientific and historical interest are also being made for the Congress week and the following week.

This is a preliminary notice and full details will be notified later. Applications for the Provisional Programme should be addressed to the Honorary Secretary, International Congress of Physical Medicine (1952) 45, Lincoln's Inn Fields, London, W.C.2.



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PERSONAL NOTES

Dr. John W. Kennedy, Phoenix, spoke before the Gila County Medical Society, Miami, Arizona February 21, 1951. His topic was "Abnormalities of Pulmonary Physiology in the Pneumococciases."

Dr. Charles Van Epps, Phoenix, addressed the February staff meeting of St. Joseph's Hospital, Phoenix, on February 12th. His subject was "Case Presentation of Spontaneous Rupture of the Uterus." It was discussed by *Dr. O. O. Williams*, Phoenix.

Dr. R. W. Ripley, Phoenix, discussed the "Contemporary Treatment of Meningitis" at the February 19th St. Monica's Staff Meeting. *Dr. Marcy Sussman*, Phoenix spoke at the same meeting on "Unusual Cause of Metastatic Disease."

At the February 26th meeting of the staff of Good Samaritan Hospital, Phoenix, *Dr. Walter Abbott*, of Des Moines, Iowa, well-known neurosurgeon, spoke on "Complications of Head Injuries."

Dr. Marcy Sussman, Phoenix, spoke on "Lymphoblastoma of the Stomach" with presentation of four cases, and *Dr. Henry Siegal*, Phoenix, presented "An Unusual Case of Pregnancy and Fibromyoma of the Uterus," at the Good Samaritan Staff Meeting.

Dr. Jeffrey A. O'Connor, Phoenix, has reported for duty with the medical department of the army at Fort Ord, California.

Dr. Joseph Baer, Chicago, Professor Emeritus of Obstetrics and Gynecology, Rush Medical School, Chicago, and Immediate Past-President of the American Gynecological Society spoke on "Endometriosis" before the March 5th session of St. Joseph's Hospital.

At the annual midwinter conference of the Los Angeles Radiological Society, *Dr. Marcy L. Sussman*, Phoenix, discussed a paper of *Dr. E. B. D. Neuhauser*, Boston, Massachusetts, on "Congenital Malformations of the Heart and Great Vessels Amenable to Surgery."

Mr. Joseph Donovan, Executive Secretary, Santa Clara County Medical Society spoke before the March 12th meeting of the Maricopa County Medical Society. He was in Phoenix at the invitation of the Maricopa County Medical Society to make a survey and recommenda-

tions for a public relations program for the Maricopa County Medical Society. Such a program was approved by vote of the Society membership following the talk and discussion and a sixty-dollar annual assessment of the membership approved to finance the program.

Dr. J. F. McCahan, Assistant Secretary of the Council on Industrial Health of the American Medical Association, spent the day of March 13th in Phoenix discussing the Industrial Hygiene Program of the American Medical Association with officials of the State Medical Association and the State Department of Health.

In the morning *Dr. McCahan* conferred with *Dr. J. P. Ward*, Director of the State Department of Health regarding the Industrial Hygiene activities of the State Health Department. At luncheon he met with *Dr. Frank Milloy*, Secretary of the State Medical Association, *Dr. C. H. Gans* of Morenci, Chairman of the Industrial Relations Committee of the Arizona Medical Association, and *Dr. R. S. Haines* of Phoenix, member of the Industrial Relations Committee, and *Dr. Ward* to discuss the part that private physicians should play in the prevention of industrial health hazards. *Dr. McCahan* stressed the importance of private physicians being alert to industrial dangers not only as they regard accidents, but also as a cause of illness.

In the afternoon *Dr. McCahan* discussed further possibilities of increased industrial hygiene activity with *Dr. Gans*, *Dr. Ward*, and *Mr. Harry Jordan*, the Industrial Hygiene Engineer for the State Department of Health.

Before coming to Phoenix *Dr. McCahan* had visited in Texas and New Mexico conferring with officials of the State Medical Associations and the State Departments of Health regarding Industrial Hygiene Programs. In the afternoon *Dr. McCahan* left for Los Angeles to continue his meetings with those physicians interested in the Industrial Hygiene Program in California.

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Mrs. Arthur A. Herold, President, 1950-51

Our President, Mrs. Arthur A. Herold, was born in Shreveport, La., and attended school there until she was ready for college. She is a graduate of H. Sophie Newcomb College of Tulane University in New Orleans, La. On Jan. 24, 1912, she married Dr. Arthur A. Herold, also a native of Shreveport. They have four children, three sons and a daughter. She organized her local Auxiliary in 1928 and her State in 1929. She is past president of the Southern Medical Auxiliary, as well as of her Parish and State Medical Auxiliaries. She has been on the National Auxiliary Board since 1931.

YAVAPAI COUNTY NEWS

Yavapai County Auxiliary had their annual rummage sale for their welfare fund on Feb. 16 and 17. The money thus raised will be used to cover whatever donations they make to both local and national welfare causes. They also collected enough money at their last meeting to buy sheets and window shades for the Prescott Salvation Army dormitory, and when a local family was burned out several weeks ago, they provided quite a few necessary items for their new home.

MARICOPA COUNTY NEWS

Maricopa County Auxiliary is well represented on the various committees which are putting over the very big project of getting every person over 15 years of age in Maricopa County to have a chest x-ray. This project under the auspices of the Maricopa State Health Department will cover many months and the Doctor's wives are working along with their husbands and members of many other organizations to make it a big success. The meeting, held on March 12th at 8 P.M., was a dessert bridge affair with a short business meeting and the emphasis on meeting and greeting old and new members.

GILA COUNTY NEWS

Gila County Auxiliary, though small in size, makes great plans and carries through with them. At a recent meeting they voted to send a check for \$446.19 to Mr. Craig, Superintendent of the Gila General Hospital for the furnishing of a corner room in the new hospital. A bronze plaque on the door of this room will give the name of the Donors.

They also plan to investigate the possibility of sponsoring a series of radio programs on the local radio station. A benefit card party and tea will be held by the members on Wednesday, April 11th at the Country Club. This small group also was 100% subscribed to Bulletin and "Today's Health."

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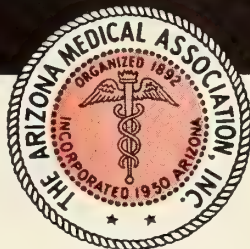
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(1) Mann, G. V., and Stare, F. J.: Nutritional Needs in Illness and Disease, J.A.M.A. 142:409 (Feb. 11) 1950.

(2) Stieglitz, E. J.: Hypertensive Arterial Disease and Hypotension, Chapter 30, Geriatric Medicine, The Care of the Aging and the Aged, 2nd ed., Philadelphia, W. B. Saunders Company, 1949.

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VOL. 8, NO. 5



MAY, 1951

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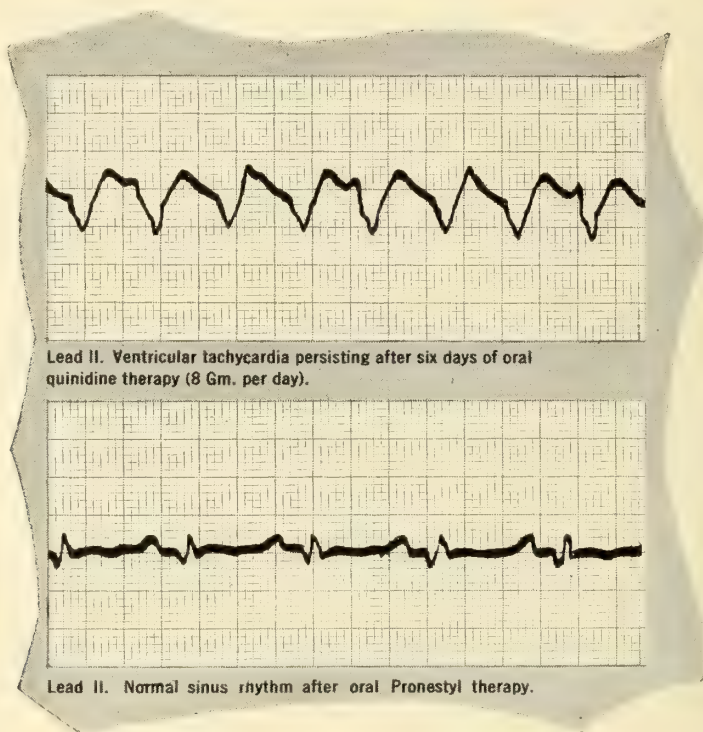
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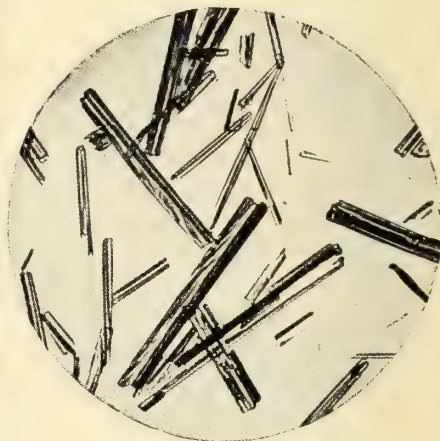
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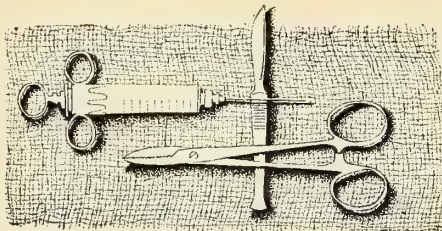
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34%	0.078%	
mg.	768 mg.	per qt.
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mg.	512 mg.	per qt.
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mg.	750 mg.	per qt.
0.18%	.00082%	
mg.	8 mg.	per qt.

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Complete information and a trial supply may be obtained upon request. BREMIL is available in drugstores in 1 lb. cans.

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4. Recommended Daily Dietary Allowances, Revised 1948, Food and Nutrition Board, National Research Council.

palatable, easy to prepare

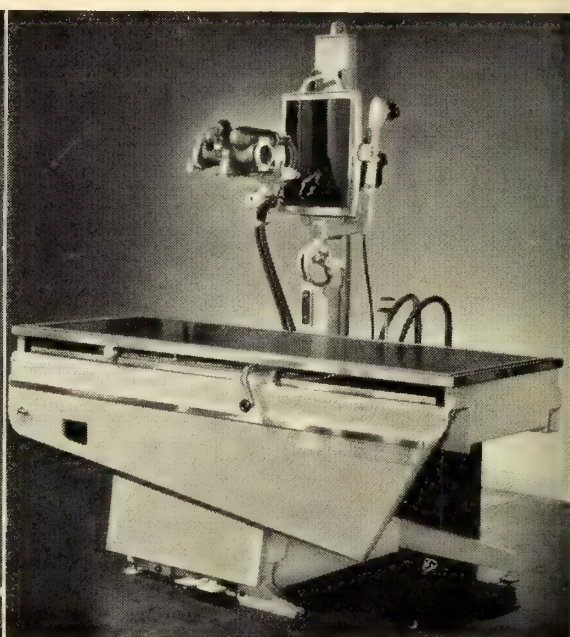
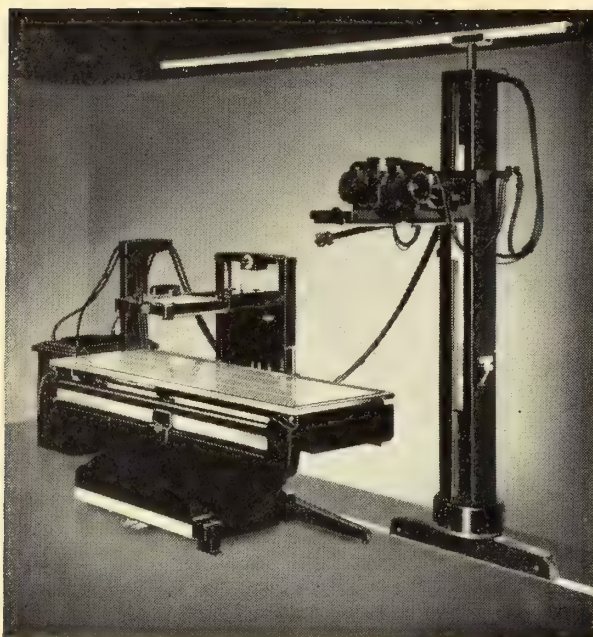
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Gray, L.: J. Clin. Endocrinol. 3:92 (Feb.) 1943.

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*Linsell, W. D., and Fletcher, A. P.:
British M. J. 2:1190 (Nov. 25) 1950.

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From The Literature

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- Paul and Montgomery, J. Iowa State Med. Soc., June, 1948.
- Krantz, Holbert, Iwamoto and Carr, J.A.Ph.A., Vol. 36, pp. 248-250, 1947.
- New and Non-official Remedies, 1950, p. 285.



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References:

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Head Pain as a Diagnostic Lead

Frequently the presence of head pain is overlooked. The physician learns of it only if he has made an effort to elicit the information. Since the etiology of the pain is the basis of rational management, the patient should be warned against taking medication before diagnosis is made.

Friedman¹ deplores the tendency to call any chronic recurring headache migraine. Careful history-taking and full physical and neurological examinations are essential for accurate diagnosis. A good starting point is a description of the headache — its character, laterality, frequency and intensity.²

The following chart gives briefly the primary diagnostic leads and treatment for the most common types of headache.

Etiology of Headache	Primary Diagnostic Data	Primary Therapy
Inflammatory e.g., Meningitis Abscess	Inflammation of intracranial structures; fever; leucocytosis; bacteriologic diag.	Specific: sulfonamides and antibiotics. Symptomatic: analgesics.
Tumor	Pain varies as spinal press. changes; skull X-ray.	Specific: surgery. Symptomatic: analgesics &/or hypnotics.
Sinusitis	Sinus congestion and infection; cloudy X-ray.	Specific: antibiotics and drainage. Symptomatic: analgesics.
Hypertensive	Hypertension present but pain not related to b.p. level; Di-hydroergotamine relieves pain.	General hypertention therapy; sedation. Symptomatic: analgesics.
Migraine & other vascular headaches	Headache: recurrent, intense, throbbing. No organic causation; migraine in family; patient: energetic, perfectionist. Visual prodromata; g.i. upset during headache.	To abort attack: oral ergotamine plus caffeine. General: adjustment to minimize nervous stress.

Data here tabulated is from: Wolf, G., Jr.,³ and Friedman, A. P.⁴

Cecil⁵ ranks vascular headaches, e.g., migraine and tension headaches, as the most commonly encountered of all. Because of their functional nature and usual recurrence at frequent intervals, they present a long-term therapeutic problem.

Therapy is conducted along two lines:

1) *Psychotherapy to reduce the frequency of attacks. This consists mainly of advice on emotional adjustment to stressful situations and guidance toward a good balance between work and relaxation.*

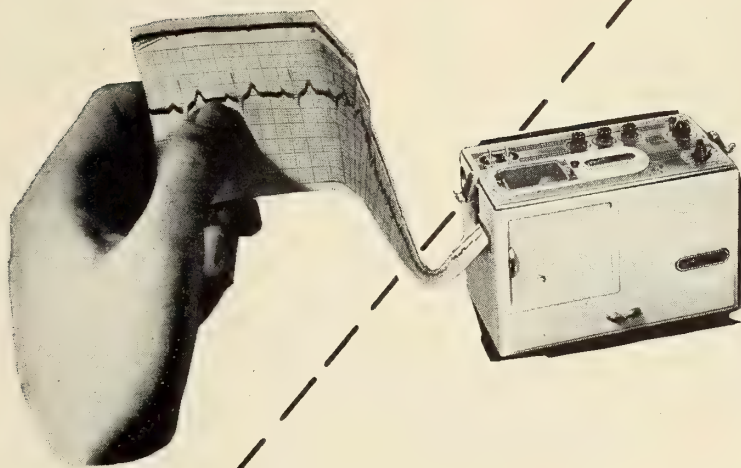
2) *Treatment of the distressing attack to prevent the usual period of incapacitation. Many investigators have reported that ergotamine preparations are effective for relief of the acute migraine attack in 80% of cases.^{1,6} The drug is given immediately when an attack is approaching and dosage adjusted to the needs of the individual.*

1. Friedman, A. P. and von Storch, T.: 99th A.M.A. Session, June 1950. 2. Butler, S. and Hall, F.: M. Clin. N. Amer., p. 1439 (Sept.) 1949. 3. Wolf, G., Jr.: M. J. 54:23, 1951. 4. Friedman, A. P. and Conn, H. T.: Current Therapy, 1950, p. 563; Saunders Co., Phila. 5. Cecil, R. L.: A Textbook of Medicine, ed. 7, 1948, p. 1483; Saunders Co., Phila. 6. Horton, B. et al: Staff Meet. of Mayo Clinic 20:241, 1945.

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President's Page



HARRY THOMAS SOUTHWORTH

Harry Thomas Southworth, born in Prescott, Arizona on June 19, 1904, son of an Arizona Physician who was President of the Arizona Medical Association in 1922.

Dr. Southworth received his Bachelor of Science Degree from the University of Idaho in 1928 and his Doctor of Medicine Degree from Rush Medical College in 1933.

He practiced in Jerome, Arizona in the year 1934 to 1938. Then moved to Prescott, Arizona in 1938 up till the present time.



I accept the office to which I have been elected with a deep sense of responsibility. I shall make every effort to fulfill the duties of this position to the best of my ability.

It is not the intent of your President to set a course to be followed, nor is it possible to foresee the problems that lie ahead. There are, how-

ever, certain unmistakable challenges which we must accept.

During the past few years, organized Medicine has had an uphill fight to maintain its freedom in our democratic nation. It was the intent of the administration to openly sell the public a "bill of goods" in the form of socialized medicine. Fortunately, we were able to stem the assault. Other tactics will now be used and well prepared plans are available to the champions of this project. The administration has not given up the fight. There are still those in the administration who have the time to carry on while their colleagues fumble with international policy and world problems, bewildered and confused. This time, the issue may come rapidly under the guise of a National Emergency Measure, or it may be insidious and follow a long range policy of propaganda, whatever the strategy, we must remain alert.

We must continue to give our whole-hearted support to our voluntary prepayment medical plans. There will always remain one of our best lines of defense.

During the months ahead, our profession will be called upon for more and more men for the armed services. This may follow the well laid co-ordinated plans now in operation, unless we repeat our past experiences, in which case the urgency of mobilization will of necessity disregard any semblance of planning.

Our time and support will be needed for Civil Defense. It is to be regretted that such plans are not already in a working stage throughout the nation. Is it possible that we must await another Pearl Harbor to incite our enthusiasm for such a program?

The course of events during the past few years has spot-lighted the practice of medicine, bringing every act of each member of our profession under close public scrutiny. Now, at a time when the entire nation is bemuddled

and is suffering from indecision, is casting about for strong leadership and confidence, and when investigations are the order of the day, it is time for our own organization to evaluate its status and for us to see that our house is in order. There is no place in the practice of Medicine today for anyone who is so self-centered and selfish that he neglects his obligation to his community and to his profession. This is a time for cool thinking and calculated decisions. Let each of us begin with a self-investigation. Are we sincere, just and ethical? Let us correct the faults we are bound to find, and then when we are satisfied with our individual

qualities, let us consider our worth to our local, state and national organization. Is our attitude constructive, or do we tend to be destructive and to block every effort of our associates unless it fits into our own scheme? It is only through individual improvement and strong individual support that we can hope to have a compact, sturdy organization.

If the basic requirements of our profession are attained, we need have no fear of our standing as citizens.

When the challenge comes, let us be united and ready.

ORIGINAL ARTICLES

AN EXPANDED USE OF STREPTOMYCIN AND PAS

WILLIAM H. OATWAY, JR., M.D.*, AND FRANKLIN REDING, M.D.**

Streptomycin became available for clinical use about 5 years ago, and the PAS compounds were put to use in the United States only a little more than 2 years ago. There are many things left to say about their use, about the interpretation of results, and there are quite a few problems left to solve.

In the early days the use of streptomycin was determined by the small quantity available, the cost, the urgency of need, and the unproved chance that it might be effective.

The exact usage was not certain, and the path ahead was not entirely clear in November 1949, fifteen months ago. The chief problems arose from the *fear of resistance, the fear of toxicity, the uncertainty about dosage schedules, the possible need to use a PAS compound, the uncertainty as to the best form of PAS, and the apparent need to defer therapy until more urgent times.*

In order that the staff at Barlow Sanatorium might take a more enlightened attitude, it was decided to survey each of the questionable points as it affected the treatment of patients at Barlow. Part of the information was obtained from the literature and correspondence with

other workers; part came from the results of clinical studies at Barlow; and part came from the intensive study of the early streptomycin-treated cases at the hands of Dr. C. R. Smith and colleagues in the Barlow Laboratory.

There was a considerable percentage of patients who were making no progress in the last step towards becoming non-infectious. There were hundreds of persons being diagnosed as tuberculous in a community x-ray survey, and the sanatorium waiting list was becoming impossibly long. Action was needed.

After the preliminary study of the problem a small report was made to the Barlow staff, including a summary of previous bacterial sensitivity tests. A case was made in answer to the question, "Can the Indications for Chemotherapy in Tuberculosis be Widened?" *The thesis that such a course was safe and possible was accepted by the staff.* It was decided to start treatment of those patients in the sanatorium, and those admitted during the next three months, whose status fit the new criteria. It was also decided at the same time to study the use of a PAS compound, PASNA; to continue to observe the sensitivity of tubercle bacilli to streptomycin and PAS; and to observe the clinical progress of the newly selected group 6 months after the end of treatment.

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**Assistant Medical Director, Barlow Sanatorium, Los Angeles.

Some of the data came from fairly small numbers of patients, especially that on the clinical effect of the drugs, but in general it seems worth while to add the information to that which is accumulating. The Barlow work is supplemented by data from La Vina Sanatorium, obtained in the past ten months.

It is timely that this report comes just after the Atlanta conference on streptomycin of the Veterans Administration and the American Trudeau Society. Two of their major papers were published last month.

1. *Early Studies of Resistance to Streptomycin at Barlow—*

A search for resistant strains was begun at Barlow Laboratory as early as the fall of 1947 by Dr. C. Richard Smith and staff. They tested sputum and gastric specimens from all patients and ex-patients who had been given streptomycin up to that time. Those cases with resistant strains were tested repeatedly afterwards.

In January 1950 a summary was made of the sensitivity tests. *Specimens from eighty-seven ex-patients* had been repeatedly studied for resistance. *Fourteen cases*, or 16 per cent, showed varying degrees of resistance. Two were listed as 'slight'; six were 'moderate' (tho three reverted later to 'slight' or 'no resistance'); and six were 'greatly resistant' (tho two reverted to 'slight' or 'no resistance'). One of the latter patients developed a strain which was dependent at 1,000 gammas.

A second group was composed of *fifty-one of the patients in the sanatorium* at that time. Only *three cases*, or 6 per cent, had specimens resistant to some degree; in two it was 'slight' and in one it was 'moderate'. These were all re-admissions or holdovers from a previous era. It was obvious that the inpatients were relatively less resistant than the ex-patients who were treated earlier and with larger doses.

Correlation of the resistant cases with the use of PAS compounds disclosed some encouraging news.—No ex-patient with a resistant strain had had PAS during the major part of his therapy. No in-patient with resistance had previously used PAS.

2. *Concerning Dosage Schedules—*

Barlow Sanatorium had used small doses of streptomycin since 1948. In conjunction with Dr. Bogen's imaginative work, this was a West-coast innovation. It has been confirmed by the large scale V.A. symposia, with the stipu-

lations that tho the use of half a gram per day is less toxic, less costly, and produces less resistance, it also produces slightly less satisfactory clinical results than larger doses.

We also decided to try an intermittent dosage, giving 1 gram twice a week in single doses. A PAS preparation was given daily.

The same sized doses of SM have been used for all patients, irrespective of body weight. 3. You are all familiar with the *streptomycin versus dihydrostreptomycin controversy*. Much convincing material has been published on both sides. The latest data suggest that the dihydrate may be the more toxic, after considerable usage, on the auditory rather than the vestibular portion of the eighth nerve. The sulfate is a much safer drug than the hydrochloride.

In the summer of 1949 Barlow shifted from SM to the dihydrate, then shifted back to SM in the fall. Within a few weeks three patients developed severe vertigo. It may have been a less pure lot, since the dosage was the same. An immediate second shift to dihydrostreptomycin was made, and it has been used at Barlow and La Vina ever since, tho a further change is being considered.

Using the small or intermittent doses, with relatively small totals, there has been no clinical eighth nerve damage at Barlow in 140 cases since then, nor in the 75 cases whose course has been completed at La Vina.

A pseudo-vertigo should be mentioned. We noted five patients who developed typical vertigo while receiving DHSM and PAS. This sometimes occurred in the first 2 weeks, some times with symptoms of intestinal irritability. All symptoms cleared when PAS was withheld, tho it required five days in one case. All were able to continue taking both drugs.

4. *Progress in the Use of PAS Compounds—*

Para-amino-salicylic acid was first used at Barlow in January 1949. It was a powder, contained impurities, and tended to decarboxylate and become more toxic than usual in a few days or weeks. Thirty-four cases received it in ten months, and 55 per cent had a tolerance labelled 'fair' or 'poor'. The total intake aimed at 16 grams in four doses, but often hit only 8 to 12 grams.

Blood levels were determined on a number of patients, but the level did not depend on the dose nor on the tolerance, and since no one knew the effective level and since the test was

time-consuming, it was abandoned. A summary was made of the clinical effect, but no conclusions could be drawn, since the series was too small, and all but two patients received streptomycin at the same time.

In November 1949, after a preliminary trial, PASNA was given instead of PAS. Ninety-two began its use in the next five months. PASNA is a trade preparation of sodium para-aminosalicylate, in granule form, coated with stearic acid. The composition of the granule is 71 per cent PAS, 28 per cent sodium and moisture, 1 per cent stearic acid. It is easy to take, and usually goes thru the stomach before the coating is dissolved. Only 20 per cent of the patients have slight and inconstant gastric symptoms; about 5 per cent may vomit at times; and about 20 per cent may have loose stools. Discontinuance is rarely necessary because of intolerance. PASNA is easier absorbed, both because it contains sodium PAS and because the intestinal irritation is less. Dr. Smith confirmed the work of San Francisco workers (Brown, Hinshaw, and Roberts) that the blood level reached 5 mgm. per cent or more at two hours.

It was reported by patients that the granules were going thru into the stools, so a check was made on several occasions by 30 patients, as well as by the nurses. Half of the patients noted 'shells' inconstantly, and they proved to be 'ghost granules', with most of the powder absent. There was no correlation with the intestinal symptoms nor, in a few cases, with blood levels.

PAS and PASNA were usually given for 6 weeks to 4 or 5 months. Resistance tests to PAS were done on cultures from several of those cases which had received PAS the longest, but they were negative. Dozens of tests have been made in the year since then and *no resistant culture has been found*. The instability of the test-drug makes the test quite delicate. Several of the Barlow patients showed varying amounts of resistance to 10 and 25 gamma on one test, only to have later specimens show complete sensitivity. If resistance tests are necessary after use of PAS (and there is some evidence that tests are redundant) they should always be repeated on a new batch of media.

In addition to intolerance and resistance to PAS drugs there is a third hazard,—*specific sensitivity*. A small number of cases has now been reported from Mayo's, by Roberts, by Rogers,

etc. We encountered three cases at Barlow, or an incidence of 2.4% of 125 cases, and two cases at La Vina, or an incidence of 2.5% of 80 cases receiving the drugs. All five cases were reactive to PASNA, and three were tested and reacted to PAS. Two had fever and malaise, two had fever, flush, and malaise; one had fever, malaise, dermatitis, and finally asthma. The drug usage was stopped in the Barlow cases, but the La Vina cases have been desensitized, using the method of Dr. Roberts (starting with 1/10 gram TID, increasing 1/10 gram every third day). After stumbles due to eagerness, the full clinical dose has been accepted in both patients. We have used PASNA for the purpose, since it is easier to weigh the granules.

In early 1950 it became certain that 'PAS' should be replaced by 'sodium PAS'. The latter drug is more stable, does not decompose for months, is more easily absorbed, and it is apparently purer. Barlow Sanatorium has continued to use PASNA; La Vina Sanatorium uses plain sodium PAS for all of those who can tolerate it without too much discomfort. If they have recurrent gastric irritation, as about 25 per cent do, we try PASNA. If there is still difficulty with toxicity, we limit the drug to the two days per week on which streptomycin is used. The patients take a full teaspoon, 3 times per day. A point in favor of sodium PAS is cost; it can be had for about 1/3 that of PASNA—or about \$10 less per month.

At one time 40 per cent of the patients at Barlow were taking PASNA. Sixty per cent at La Vina are now taking a PAS compound, and 96 per cent of the patients in residence are taking, or have taken it.

5. Protocol for the Special Barlow Study of 1949-50—

The criteria for selection of cases for an expanded use of the drugs included every case in the sanatorium—

1. *With* occasionally positive bacterial studies.
2. *Without* cavitation by several x-ray methods.
3. *With or without* collapse therapy.
4. *Without* change for 4 to 6 months of observation.

It was thought that there might be a few cases eligible in the total census of 100. A survey showed, however, that there were 25 patients eligible at once, and several more when further examinations had been made. Others were included when their cases came to fit

the criteria during the several months of study. These cases would have continued to 'mark time' unless they healed spontaneously or were treated with some form of collapse therapy.

Forty unhealing cases were treated with streptomycin and PASNA. Three routines were used, including half a gram of SM plus PASNA daily, the same routine plus a few more weeks of PASNA, and 1 gram of SM twice a week with PASNA daily. The indications for the subgroups were similar, and the results were similar so the small series will be reported as a whole.

At the end of the course of treatment 80 per cent of the patients became non-infectious. During the next 6 to 9 months the ratio of negatives and positives remained the same, tho 12.5 per cent reversed each way. *When collapse therapy* was present 84 per cent were negative after 6 to 9 months. A recent checkup has shown that, of the 8 patients who still were infectious, four have since been converted by surgery—3 by resections and one by thoracoplasty. Eight of the cases were labelled as being 'cavity suspected but not proved'; 4 remained or reverted to positive, and 4 became negative. The changes by x-ray are not worth reporting, since almost all showed improvement or lack or change.

Fourteen patients who had *small lesions*, rare positive gastrics, or a reason for not taking streptomycin were given PASNA daily for an average of 12 weeks. Thirteen became negative at the end of therapy, but three reverted to positive at the end of 6 to 9 months. (Seventy per cent had remained negative).

Sixteen cases with cavity, or probable cavitation, were treated with $\frac{1}{2}$ gm per day of SM, with PASNA continued afterwards. Only 3 became negative at the end of therapy, tho six more converted after 6 months. These late conversions were probably due to the associated collapse therapy, since 8 of the 10 patients with collapse became negative. The *recent fate* of these sixteen shows a similar situation:—all ten now doing well have had a previous or recent collapse or resection; half of those doing badly have not had added local therapy.

A miscellaneous group of nine cases had caseous-pneumonia under collapse, tuberculous tracheo-bronchitis, or cavitation. They were treated with PASNA only. All except one patient were still positive 6-9 months later, in spite of collapse therapy in most of them.

From this series, I believe that we can say that salvage is possible by the use of chemotherapy in unhealing, non-cavitative tuberculosis; that chemotherapy works best in conjunction with judicious collapse or resection; that PAS may have a slight healing function of its own; and that when an ulcerative or cavitative lesion is present, the drugs are rarely enough to produce a complete healing.

6. *La Vina Drug Usage*—

Only a few points concerning the use of chemotherapy at La Vina Sanatorium during the past year will be mentioned. The same drugs and routine are used as at Barlow.

Forty patients have been discharged, of which 82% received streptomycin and PAS, and 8% more received PAS only. Exactly half had collapse therapy, half did not. 80% of those who did *not have therapy* were negative by one or more gastric cultures. Eighty-eight per cent of those who had collapse therapy or resection were negative by 1 or 2 gastric cultures.

Fifty patients are in residence. All but one (or 98%) have been given both drugs.

It should be mentioned that four patients had positive *gastric culture relapses* after discharge, 3 to 5 months after drug therapy ceased, but all left before the optimal time. One patient in the sanatorium had a relapse by x-ray, and two by gastric cultures; they seem to respond to further drug therapy. None of these had received the prolonged intermittent routine.

It can be seen that the La Vina use of chemotherapy has been on a *variety* of cases. Its aim has been the therapy of all cases in which a proved multiplication of bacilli exist, and the drugs have been used from the start of sanatorium care, with or preceding whatever form of collapse or resection therapy is possible. The results seem good so far, and the longest use with the least drug seems the best.

7. *Resistance to Streptomycin Since January 1950*—

A further late checkup was made on the sensitivity tests at Barlow from January 1950 thru April 1950, during the time when numerous patients were started on streptomycin and a PAS compound. *No case from that era* developed a resistant strain by the end of the period, nor by September 1950, six month later. A survey was again made two weeks ago of the 99 cases from the first 9 months, as well as the

49 in the next five months. *No instance of significant resistance has occurred*, either to streptomycin or PAS. The low total dosage, the brief periods of treatment, and the use of PASNA could be responsible.

A point of interest is the difficulty which even an experienced laboratory may have in doing large numbers of the delicate sensitivity tests. Almost all of the plates containing 10 gamma of SM which were made at Barlow between late July and mid-September, 1950, showed the same growth as the controls. A few specimens with scanty growth showed only 10% resistance. Cultures at 25 gamma did not show resistance. *Sub-cultures or new specimens* from those patients showed that 4 of the 6 with 100% resistance and 5 of the 8 with 10% resistance showed no resistance on the later tests. The ones not retested have mostly become negative by culture because of spontaneous or surgical conversion.

A late study of the patients who had received large amounts of streptomycin in the early days is interesting. Seventeen had received 115 grams or more, for an average of 163 grams, and a high dose of 271 grams. Bacterial studies were available on all patients. Only one patient, with tracheo-bronchitis, became regularly negative in the few months after streptomycin was used *without collapse therapy*. Two became negative with *concurrent collapse therapy*. One became negative later with long-continued rest. However, *eight* became (and are now) negative *when collapse or resection therapy was added at later dates*. It is probable that several of these patients were conserved for the later definitive surgery by the use of the drugs.

It was possible to test eleven of the seventeen for resistance. Two had slight resistance, but one of them healed her disease; one developed resistance, lost it, and regained it with later therapy; a fourth had a moderate resistance across the board. These cases amount to only 36% of those which could be tested, or 23% of the entire group. It would seem that *considerable streptomycin can be given without loss of sensitivity*, even without accompanying PAS.

DISCUSSION

Resistance to streptomycin has formerly seemed to be a serious obstacle to extensive use of the drug. The literature has shown a decrease in the emergence of resistance with the use of smaller single doses, a lower total dosage, and the combined use of a PAS preparation. The

The recent V.A.-N.T.A. conference, and our own work, have shown that the drugs may be used widely if carefully, with almost no loss of sensitivity. No one has had a greater phobia concerning resistance than Oatway, who in 1947 wrote a 'letter to the editor' of the Journal of the American Medical Association, warning physicians against the effects from careless use of streptomycin, both to the patient and to his contacts. Yet three of the men who joined me in the warning at that time are inclined to join me now in the belief that care and caution can be combined for a wider early use of the drugs.

Tests of cultures for streptomycin and PAS sensitivity are delicate and difficult even in expert hands. They probably are of little need or value except in long-continued use of the drugs. There are recent suggestions that such tests be dispensed with, but at some times it is better to know than to be fooled.

Chemotherapy may be used early in almost every type of lesion and in every stage of disease. This should include infectious minimal lesions, especially when exudative. The 250 physicians who took part in a judging contest last spring in Washington recommended chemotherapy for 64 per cent of the cases examined, but only for 17 per cent of the minimal cases, and only for 27.6 per cent of those with worsening minimal lesions. This could be called too little, too late.

The toxicity of streptomycin and PAS has been sufficiently discussed. We seem to need more information, however, on the difference between streptomycin and the dihydrate, since only the better drug should be used. We need to know the optimal single, daily, and weekly amount of PAS which should be used.

Further comments on dosage can not be made with certainty. There is no final proof that soaking the tissues at long intervals is better than maintaining a lower concentration more constantly. The low or intermittent dosage schedule has been safer, effective, convenient, and inexpensive.

The conclusions which were brought to us from the Atlanta Conference in February were as follows—

1. The best healing effect at present seems to result from 1 gram of streptomycin daily for 4 months, combined with 12 grams of PAS daily, or 1 gram of SM, twice a week

with PAS daily. The biweekly method would have the advantages of less resistance, greater convenience, and lower cost.

2. Daily PAS is better than biweekly PAS.
2. It is not certain whether large early doses of SM are needed, or whether small doses are as good as large. There is also a controversy as to whether the dosage for acute disease should be large, or whether it should be given biweekly or daily.
4. Cases with some loss of sensitivity to streptomycin may legitimately be retreated.
5. Chemotherapy may seal off secretions and caseation. Bacilli may become 'quiescent'.
6. Prolonged therapy may be of special value.
7. Chemotherapy plus collapse therapy is best. Streptomycin and pneumoperitoneum are good therapy for tension cavities.

The results which I have described from California, plus the work of others, suggests the *value of combining the drugs with some form of local treatment*. This is especially indicated when the lesion is caseous or cavitated. Chemotherapy may not be decisive when collapse or resection cannot be used for destructive lesions. Failure to convert the bacterial findings in the absence of resistance or a bronchial lesion should suggest a cryptic cavity. The actual appearance of lesions in resected lungs impresses, or even shocks one anew, with the seriousness of any necrotic lesion, with its often comparatively benign appearance by x-ray, with the need for early containment by drugs, with the need for help from collapse or resection therapy, with the folly of using drugs alone for long periods, and with the attractiveness of using resection to remove the bulk of the disease. The 'necrosis factor' tends to keep the lesion unhealed and the patient recurrently infectious.

The *duration of chemotherapy* should be decided by close observation and good judgment. A reversible collapse procedure should be used as soon as indicated; surgical collapse or resection should follow, if needed to put the disease in a better position to deal or to rid the body of the lesion. Chemotherapy and pneumoperitoneum is a valuable pair when the disease is bilateral or acute, but its progress should be observed most carefully for further needs.

It is hard to push ahead in a situation which is doing *fairly* well, but which really needs further action.

'Drug relapses' may occur in the months after drugs have been discontinued. They may be either bacterial or by x-ray. They are probably due more to brief therapy and the presence of necrosis or cryptic cavitation than to strain or low personal resistance. They can usually be managed by a searching x-ray study of the lesions, by prolonged drug treatment, and by the addition of the most helpful collapse or resection measure.

Streptomycin should always be accompanied by a PAS compound. It is possible to give PAS to almost any patient, since toxicity and irritability may be avoided by use of a sodium compound, a coated granular preparation, and desensitization in case of specific reactivity. The use of a PAS compound by itself has been of help only in small lesions without evidence of destruction.

A *better routine* than the one now available will probably be described. Better drugs may be described, but they are not at hand. We like small doses, intermittent dosage, and a more prolonged course, tho we have not used weekly SM, biweekly PAS, subcutaneous PAS, benamide to delay excretion of PAS, nor injections of combined SM and PAS. The trial of weekly doses of SM and PAS will be watched with hope and eagerness.

The '*test series*' of unhealing, non-cavity cases which was treated at Barlow Sanatorium was a fairer trial of the drugs than acute lesions or advanced destructive disease, tho the courses were too short. It seems to have been well worth while in salvage of patients, as well as in experience for their physicians.



JAUNDICE

PHILIP THOREK, M.D., F.A.C.S.
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Jaundice, or hyperbilirubinemia, is an important subject to both the general practitioner and specialist alike; it always presents an interesting diagnostic problem. To have ways and means of coordinating and simplifying the subject is imperative so that with the diagnostic armamentarium at hand a diagnosis may be readily reached and proper therapy instituted. A thorough knowledge of the pathologic physiology involved results in a more rapid and accurate diagnosis than does the memorized knowledge of the hundred and one conditions which might be associated with this symptom. It is with this in mind that the subject is presented.

PHYSIOLOGY

The fate of a normal red blood corpuscle seems to be the proper approach to the understanding of icterus. It is recalled that the normal erythrocyte eventually terminates its existence by being broken down in the spleen. In this organ the disintegrated red cell is divided into an iron containing part (hemosiderin) and an iron free part (hematoidin). The iron free part is the precursor or mother substance of the main bile pigment called bilirubin. As the iron free part of a broken down red corpuscle is delivered from the spleen to the general circulation it comes in contact with the reticulo-endothelial system which is a specialized network of cells arranged around the vascular system. These cells have the ability of converting the iron free part of the red cell into bilirubin. This bilirubin is attached to a heavy protein molecule, hence it is designated as bilirubin proteinate. It is in this form that it is delivered to the liver. The liver splits the bilirubin proteinate and excretes pure bilirubin via the hepatic duct into the gallbladder. When the gallbladder contracts, bilirubin is delivered into the intestinal tract where it is acted upon and broken down by bacteria to its end metabolite known as urobilin (urobilinogen). Some of this urobilinogen passes out and colors the feces; the remainder is absorbed from the intestinal tract and is carried back to the liver via the portal system. One of the many liver functions is to reconvert the

end product urobilin back to its early predecessor bilirubin.

To thoroughly comprehend and clinically classify jaundice, one must understand this physiology and continually keep in mind the difference between bilirubin and urobilin.

CLINICAL CLASSIFICATION

Many classifications have been presented, each having their respective good points and drawbacks. A classification which has served as well is one which divides jaundice into:

1. Prehepatic
2. Intrahepatic
3. Posthepatic

In this way we can place the lesion as to its location before the liver, in the liver, or after the liver.

PREHEPATIC JAUNDICE

In icterus which develops from a prehepatic lesion the pathology may be found in the red blood cell. A typical example of this is familial hemolytic icterus. In this condition the red cells are apparently defective and instead of being the usual normal biconcave disks appear as "golf-ball" red cells. They are also smaller than the normal cell, hence the condition has been referred to as microcytic spherocytosis. These cells have an increased fragility and rupture easily. As a result of this exaggerated bursting process an excessive amount of iron free pigment is excreted by the spleen, resulting in an excessive amount of bilirubin proteinate, which is formed by the reticulo-endothelial system. This results in jaundice due to the hyperbilirubinemia. However, since this bilirubin is in the form of a proteinate and since this molecule is too heavy to pass through the kidney the urine does not show the color that one would expect in the jaundiced patient acholuric jaundice). Since an increased amount of bilirubin is being delivered to the liver, a greater amount of bilirubin is excreted into the intestines; this results in an increased formation of urobilin in the intestinal tract. This large amount of urobilin is not only excreted in the feces, but the remainder is returned to the liver. The liver converts as much of this as it can into bilirubin, but the remainder overflows into the urine, resulting in an increased urobilinuria. Should the

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Ehrlich aldehyde test for urobilin be applied to such a urine, it would be strongly positive; however, liver function tests would be negative. The van den Bergh test is of some value here, since a prehepatic jaundice gives a positive indirect and negative direct test.

Other examples of prehepatic jaundice are icterus neonatorum and hypersplenism. In the former, too many red blood cells are destroyed and in the latter the spleen is hyperactive.

INTRAHEPATIC JAUNDICE

In this type the pathology is located in the liver. It must be remembered that the entire liver does not become involved at once; if this were to occur death would promptly ensue. Any toxin be it chemical or bacterial or any organism may so injure the liver that one or more of its important functions might be interfered with. Typical examples would range anywhere from a simple catarrhal jaundice to a fulminating acute yellow atrophy. When the liver is damaged one or more of the liver function tests show signs of hepatic dysfunction. The literature is replete with various liver function tests, and to attempt to utilize many of these is most impractical. Many workers in this field have their favorite test or group of tests; at times we use some of them but for practical purposes we prefer to confine ourselves to the aldehyde test for urobilinogen, and the cephalin flocculation test of Hanger. If the lesion producing the jaundice is an intrahepatic one, then both of these tests are found positive.

POSTHEPATIC JAUNDICE

In jaundice caused by posthepatic pathology we assume that the pre- and intrahepatic functions are progressing normally. The most common examples of posthepatic jaundice are: common duct stones, carcinoma of the common and hepatic ducts, carcinoma of the head of the pancreas, and metastases to the porta hepatis.

The obstruction to the flow of bile into the intestinal tract may be partial or complete. If the obstruction is partial then some bilirubin gets into the intestinal tract and this would be converted to urobilinogen. That urobilinogen which returns to the liver will be reconverted back to bilirubin since the lesion is not an intrahepatic one, and the aldehyde test for urobilinogen will be negative. If, on the other hand, the obstruction to the outflow of bile is

complete then no bilirubin gets into the intestinal tract and no urobilinogen is formed, therefore, the aldehyde test will again be negative. Liver function tests in posthepatic jaundice reveal normal functioning livers unless the jaundice has been present well over a month and is of a severe degree; a biliary cirrhosis then forms.

DIAGNOSIS

Since diagnosis constitutes the most important part of all medicine, no detail must be overlooked. In evaluating the diagnostic possibilities of each case nothing can replace the recording of a careful and accurate history. A detailed and keen physical examination is equally revealing. It must be recalled too that although most cases of jaundice can be categorized into pre, intra, and posthepatic jaundice, there may still be an overlapping of these lesions. For example: as Watson, Popper and others have emphasized, obstructive jaundice may also be associated with intrahepatic pathology; such cases are assumed to be "cholelithic" lesions. By the same token, a true posthepatic obstructive jaundice may be present for a period of three to four weeks or over, the result in liver damage producing a biliary cirrhosis. The true clinician and alert surgeon keep such possibilities constantly in mind. Couvoisier's law is helpful. It states that a large gallbladder in the absence of jaundice usually suggests a cystic duct obstruction (mucocele of the gallbladder), a small gallbladder plus a jaundice usually indicates a stone in the common duct, and finally a jaundice in the presence of a large gallbladder speaks for a carcinoma of the head of the pancreas. One can also differentiate the various sites of carcinoma which involve the biliary tract. For example: in carcinoma of the gallbladder, jaundice is *not* present but a hard nodular mass which moves with respiration is palpable in the right upper abdominal quadrant; in carcinoma of the common duct, jaundice plus a portal vein complex (ascites, dilated esophageal varices, hemorrhoids, etc.) is present; carcinoma of the ampulla of Vater is suspected when one finds a jaundice plus signs of pancreatic insufficiency; and finally, carcinoma of the head of the pancreas can be diagnosed when jaundice plus an inferior vena cava complex (bilateral dependent edema and dilated veins of both inferior extremities) is noted.

The differentiation between a stone and a carcinoma of the common duct may not be too

difficult, however, it should be remembered that in contradistinction to the usual conception, a carcinoma may produce colic and a stone may be silent. Taking an icterus index on five successive days might clarify the diagnosis. If the lesion is a carcinoma the icterus index is high and continues to rise; however, it is possible for an icterus index to drop if there is some slight ball-valve action in the presence of a stone. Many other ways are available for differentiation and some of these have been discussed.

Unfortunately pruritus (itching) is considered to be a symptom of jaundice; this is erroneous. Pruritus is a symptom of *posthepatic (obstructive) jaundice*. When the patient's primary complaint is his itching then we feel quite positive that the patient is suffering from either a stone or a carcinoma which is involving the extrahepatic biliary passages. Rarely does a patient with intrahepatic jaundice complain of itching.

The pulse is usually slow in cases of icterus. We prefer a bradycardia in such cases, because when the pulse becomes rapid it usually forebodes an oncoming acute yellow atrophy or hepatic decompensation.

Numerous laboratory tests are at our disposal, but one can surmise that the author has a preference for the Ehrlich aldehyde test for urobilinogen, serum alkaline phosphatase, and the cephalin flocculation test. If the lesion is a prehepatic one the urobilinogen test is positive and the liver function tests are negative; if the lesion is posthepatic, both of these tests are negative. No tests are foolproof, however, the statements just made are found to be true in the vast majority of cases. It may be safe to state, however, that when a serum alkaline phosphatase is over 15 Bodansky Units, and when the total cholesterol is above 300 mg., this speaks more often for a surgical type of jaundice than a medical one.

It seems to be a waste of time, effort and money to do Graham-Cole test on jaundiced patients. The negative response found in these patients is most misleading. On the other hand, a flat x-ray film of the abdomen is always taken. Time nor space does not permit a discussion of the other tests available to the clinician; however, one should always keep in mind that since no test is foolproof diagnostic pitfalls are always present.

TREATMENT

There has been a tendency to not only classify

but to discuss the treatment of jaundice under the headings of medical and surgical jaundice; this seems both impractical and misleading. When a case of jaundice is seen one never knows whether the condition will eventually end up under a medical or surgical regime, and since both types of therapy overlap, it seems preferable to consider them together. Only the salient parts in the therapy will be mentioned.

Needless to say, preoperative care is a major factor if a case of jaundice is to be brought through a surgical procedure successfully. To mention only a few of the necessary essentials we might include electrolyte, water and protein balance, vitamin therapy, especially K, B, and C, and an adequate glycogen supply to the liver. The severe pruritus which may be associated with jaundice can sap much of the patient's strength and energy. Recently we have used intravenous procaine in a 0.1 per cent concentration and have found that this gives rather rapid and marked relief from itching in most instances. 1000 cc. of this solution are given, never exceeding the rate of 1000 cc. in one hour. A word of caution, however, should be mentioned since the drug is a convulsant, hence, its use in concentrated solutions or rapid injection of dilute solutions may produce irreparable damage. We feel that blood transfusions should not only be utilized as an operative or postoperative measure, but also as a method of supplying many of the previously mentioned needs. Preoperative laboratory tests, such as blood counts, icterus indices, prothrombin, bleeding and coagulating time, blood protein determination. A-G ratio, etc., are all of value. However, none of these replace the clinical impression gained by the seasoned diagnostician as he watches his patient through this "build-up" period.

Many operative procedures, both curative or palliative, have been described for the jaundiced patient; the type of lesion determines the type of surgery. I am of the opinion that metastases do not determine operability or inoperability; the only determining factor is fixation of the primary growth and surrounding vital structures. If the primary lesion is not fixed to a vital structure, even in the presence of operable metastases, we feel that Brunschwig's idea in attempting to remove as much of the malignant tissue as is possible is a valid one. Alexander has further stressed this point by suggesting the removal of

solitary pulmonary metastases. The monumental work of Whipple in carcinoma of the pancreas has brought those cases which were considered inoperable only a few years ago into the realm of operability.

One cannot discuss the surgical therapy of the common duct, unless he is conversant with the surgical anatomy of this structure. It is quite simple and practical to consider the common duct as being divided into four parts, each being related to the duodenum. Therefore, the common duct is divided as follows:

Part 1—Supraduodenal Portion

Part 2—Retroduodenal Portion

Part 3—Infraduodenal Portion (Pancreatic)

Part 4—Intraduodenal Portion

Regardless of where the stone is located, only Part 1 is immediately accessible to the surgeon, therefore, the incision is placed here. A stone in either Part 1 or Part 2 is usually easy to remove by means of a supraduodenal choledochostomy. I prefer to drain the common duct rather than close it, because in the presence of edema and infection one never knows when a suture might cut through. A stone located in Part 3 causes no concern if it is not imbedded in the duct wall. If the stone is freely movable it can be dislocated into Part 1 through a supra-choledochal incision. However, if the stone has become firmly fixed in an ulcerated and edematous part of the duct wall it cannot be dislodged. Some surgeons advocate mobilization of the duodenum to remove such a stone. Since this part of the common duct passes through the head of the pancreas and not between the pancreas and duodenum, and since this area is surrounded by a cage of vessels (superior and inferior pancreaticoduodenalis arteries) this maneuver seems impractical and at times is impossible. It is only of value when the stone has eroded through the duct and head of the pancreas; this is unusual. A preferable method to handle such impacted stones in Part 3 is the following: The flat x-ray film which must be in the operating room is examined; it is noted that this is a flat film and no dye has been given. If the stone is not seen on this flat roentgenogram we conclude that it is a cholesterol stone. If such be the case then a catheter, not a "T" tube, is placed from Part 1 of the duct downward to the stone; this is sutured into the common duct. In 24 to 48 hours, a few drops of ether are injected into

this catheter every morning and every evening. Since cholesterol is soluble in either most of these stones will dissolve and disappear without further manipulation. If, on the other hand, the impacted stone in Part 3 is seen on the flat x-ray film, we conclude that it is high in calcium content, and this usually is not affected by the etherization method of treatment. In such an instance a short circuiting operation is done to relieve the jaundice, which after all is of far greater and immediate importance than the presence of a stone. The procedure which we prefer is a cholecystojejunostomy. This brings up the necessity of determining whether or not the common duct should be explored. Such a decision must be made prior to doing a cholecystectomy, since if the gallbladder is removed and then one finds it necessary to do a short circuiting procedure, it usually is more difficult to do a choledochojejunostomy rather than a cholecystojejunostomy. The indications for exploring the common duct are too well known to bear repetition here. If an indication is present the common duct is explored, the necessary procedure carried out, and the gallbladder removed if there is no need for its utilization in an anastomotic procedure. A stone in Part 4 is also approached through an incision in Part 1. Occasionally such a stone will dilate the ampulla of Vater and then it can be pushed into the duodenum. If this is impossible, the middle of the descending portion of the duodenum is opened and the stone is extracted transduodenally. The duodenum is then closed.

Drains in the common duct can be removed when one is certain that bile is flowing freely into the duodenum. This can be determined by means of contrast media with the x-ray, tying off the tube, or inspecting the color of the feces. Although common duct tubes have been removed anywhere from a few days to many months postoperatively, I am of the opinion that the average common duct tube should be removed somewhere between a two and four week period.

There are cases in which it is impossible to determine preoperatively whether the condition is due to a stone or a neoplasm, and whether or not the latter is operable. Although some cases might appear inoperable preoperatively such patients should not be denied at least the chance of an exploratory operation. Occasionally a life can be saved by removing a stone

which was thought to be a neoplasm, or by removing a neoplasm which was thought to be non-resectable.

The postoperative management is as vital to a successful result as is the operative procedure itself. This part of the treatment is not relegated to the uninitiated, but is preferably handled by someone thoroughly conversant with the modern approach to this all important phase of therapy.

SUMMARY

1. The proper approach to the subject of jaun-

dice both diagnostically and therapeutically is a thorough understanding of the pathologic physiology of the metabolism of the bile pigments.

2. It has been found advantageous to clinically classify jaundice into three groups, namely, pre, intra and posthepatic.

3. Dividing the common duct into supra, retro, infra and intra duodenal portions aids in standardizing the various operative procedures applied to common duct surgery.

THE INCIDENCE OF TRICHINELLA SPIRALIS INFECTIONS IN AN ASYMPTOMATIC GROUP, AS INDICATED BY THE KLINE TEST

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Few cases of trichinosis have been reported to the Arizona State Department of Health and these have been reported since 1940. For some reasons, unknown to the authors, the cases in the outbreak reported by Andes, Greene and Breazeale (1) are not included in those records. In a state where garbage feeding of hogs is the rule, rather than the exception, it is surprising that more cases of trichinosis are not reported.

Gould (2) has pointed out, however, that "when trichinosis occurs in epidemic form it is likely to be correctly diagnosed, but when infections occur sporadically, especially if they are of mild severity, they are usually unrecognized. The disease is often difficult to diagnose clinically—and atypical cases are said to be the rule rather than the exception". In addition, many diseases may be mistaken for trichinosis. Gould (2) cites a publication of Hall (5) in which there are listed "50 diseases which have been mistakenly diagnosed in persons ill with trichinosis". Alphabetically, these range from acute alcoholism to undulant fever.

In contrast to the small number of cases of trichinosis which are reported in the United States, autopsy findings "show an average of 16 per cent infection.—This means that at least 16 per cent of persons in the United States, at the time of death, have trichinosis" (4). It should

be pointed out that these findings are usually based upon the results obtained by one laboratory technique (digestion or compression). When both methods are employed, a large number of infections are discovered. Gould (4) employed both techniques and found 266 infected individuals in 1141 autopsies—an incidence rate of 23.3 per cent.

EXPERIMENTAL

The authors were interested in determining the incidence of *Trichinella* infection in an asymptomatic group, as an index of the probable incidence of infection in the population of Arizona. After considering the various tests which might be employed for this purpose (complement fixation, precipitin, intradermal tests and eosinophilia in the peripheral blood) the method of Suessenguth and Kline (6) was selected. The technic of this method is essentially identical to the Kline test for syphilis; the antigen is an alkaline aqueous extract of dried trichinella larvae, which is converted into an antigen emulsion for the diagnostic test by the addition of 1 per cent cholesterol and 0.85 per cent sodium chloride, as in the Kline test for syphilis.

The test is performed by pipetting 0.05 ml. of inactivated serum to a Kline slide with paraffin rings, or with depressions; a small drop of the

antigen suspension is added from a syringe with a 26 gauge needle. The slide is then rotated on a flat surface for four minutes, as directed by Suessenguth and Kline (6). The results are read microscopically at a magnification of approximately 100 times, and the degree of flocculation is reported in terms of plus, as in the Kline test for syphilis.

The sera employed in this study were obtained from specimens (from residents of Arizona) which had been submitted for various serologic tests. A few had been submitted for the laboratory diagnosis of syphilis; but the majority of the specimens came from presumably healthy persons (premarital and prenatal tests, routine examination of food handlers, etc.) THERE WAS NOT A SINGLE CASE IN WHICH TRICHINOSIS WAS SUSPECTED.

RESULTS

One thousand (1000) sera were examined. the results were:

	No.	%
Negative	868	86.8
Doubtful (plus-minus or 1 plus)	32	3.2
Positive (2, 3, or 4 plus)	100	10.0

DISCUSSION

One hundred thirty-two (132) of the sera gave some observable reaction with Kline trichinella antigen; ten (10) per cent (100) gave positive reactions. Suessenguth and Kline (6) state "The flocculation reaction in the average case becomes positive about 3 weeks after infestation in man and in swine. The first positive reaction in man and in swine was obtained from the 14th-17th day to the 25th to 27th day after infestation". There is little information regarding the length of time the test might remain positive. Suessenguth and Kline (6) state, "The reaction was still not negative in man and in swine 10 months after infestation". In known clinical infections, the complement fixation and precipitin tests have usually remained positive for approximately 18 months. The results obtained in subclinical trichinosis or in asymptomatic groups are difficult to evaluate. Gould (2) cites his own studies in which "precipitin tests were performed during life in 66 persons who later came to autopsy and were examined for trichinous infection. None of the patients gave a history which suggested trichinosis. Positive precipitin reactions were obtained in 3 of 15 (20 per cent) who were trichinous and in 5 of 51 (9.8 per cent) who were nontrichinous". In

another publication, Gould (3) states that "eosinophilia usually persists six months and rarely a year after infection. It is believed that the blood precipitin test remains positive for 1 to 2 years and the immediate type of intradermal reaction may be elicited, on the average, for nearly 10 years after infection". Gould does not believe that the intradermal, the precipitin test or eosinophilia can be "relied upon to indicate the presence of old subclinical trichinosis."

It is interesting to note that 13.2 per cent of the sera (during life) reacting to some extent with Kline antigen; this compares favorably with the estimate of Gould (4) that "at least 16 per cent of persons in the United States, at the time of death, have trichinosis."

SUMMARY

One thousand (1000) sera which had been submitted for various laboratory tests were examined by the Kline slide test for trichinosis. Trichinosis was not suspected in any case. Ten (10) per cent of the sera (100) gave positive Kline tests and 3.2 per cent (32) gave doubtful reactions. These results indicate that, in spite of the relatively few cases of trichinosis reported in Arizona, the incidence of infection with *Trichinella spiralis* is as least as great in Arizona as in other parts of the United States.

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BASIC SCIENCE SEMINAR

THE RH FACTOR AND ITS APPLICATIONS

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1. INTRODUCTION

In 1940 Landsteiner and Wiener obtained an immune serum in which an agglutinable factor in human blood other than A, B, M, N or P, was determined. It was designated as the Rh factor because the serum was obtained from rabbits immunized with *Macacus rhesus* blood. Since that time several hundred scientific papers have been written concerning the Rh factor and its applications. The result of this intensive investigation has been the formulation of certain fundamental concepts. A brief review of these concepts provides an equally brief summary of current opinion on the Rh factor.

The Rh factor, agglutinogenic in nature, is primarily a property of the red blood cell. It is capable of forming antibodies when injected into a person whose cells do not contain the Rh factor, but has no normally occurring antibodies in human serum as do the A and B antigens. Although it is similar to the A-B and M-N antigens, it is inherited independently of either. About 87 per cent of the Caucasian race have the antigen present in their red blood cells and are about Rh positive, while about 13 per cent do not have the antigen and are called Rh negative. Approximately 92 per cent of the negro race, and 100 per cent of the Chinese race are Rh positive.

2. NOMENCLATURE

By 1942 a great deal was already known about the Rh factor. Landsteiner and Wiener had determined the Mendelian dominant nature of its inheritance and had postulated the existence of a pair of allelic genes, Rh and rh. The dominant gene, Rh, determines the presence and type of Rh antigen. Under this theory, Rh negative individuals are all homozygous, genotype rh rh, while Rh positive individuals could be either homozygous or heterozygous, genotypes Rh Rh or rh Rh. At the time in 1944 that Fisher and Race described the three linked gene theory of Rh factor inheritance, Landsteiner and Wiener had concluded that there were three major alle-

lomorphic or interchangeable genes and that combinations of these in the Rh pair of genes in the chromosome were responsible for the eight known Rh types. They designated the three allelomorphic genes, Rh₀, Rh', and Rh''.

Fisher and Race believe that there are three linked gene pairs in the chromosome instead of a single pair and that it is combinations of these gene pairs which are responsible for Rh type. These they have designated C, D and E, with each dominant gene having a recessive counterpart c, d, and e. The nomenclature proposed in either theory is interchangeable as shown in table I.

TABLE I

Landsteiner and Wiener	Fisher and Race	Per Cent of Caucasian bloods agglutinated by respective antisera
Rh'	C	70 per cent
Rh ₀	D	85 per cent
Rh''	E	30 per cent

The interchangeability of nomenclature proposed by Landsteiner and Wiener with that proposed by Fisher and Race.

As has been stated, there are eight possible genotypes. The approximate frequencies with which the various combinations occur are indicated in table II.

TABLE II

Landsteiner and Wiener	Fisher and Race	Per Cent of genotype occurrence in the Caucasian race
rh (neg)	c,d,e	13.0 per cent
Rh'	C,d,e	01.0 per cent
Rh''	c,d,E	00.5 per cent
Rh'Rh''	C,d,E	00.0
Rh ₀	c,D,e	02.0 per cent
Rh ₁ (Rh'Rh ₀)	C,D,e	54.0 per cent
Rh ₂ (Rh ₀ Rh'')	c,D,E	15.0 per cent
Rh ₃ (Rh ₀ Rh ₀)	C,D,E	14.5 per cent

Incidence of Rh genotypes in the Caucasian race.

Recently the presence of an antigen similar to the Rh antigen, but usually present when the Rh antigen is absent, has been discovered. It has been called the Hr factor to denote its

relationship to the Rh factor. At the present time it has been found that only agglutinogens determined by the genes Rh₁ and Rh' do not have Hr agglutinogens (Hr negative), while those determined by the genes rh, Rh₂, and Rh₀ are Hr positive, see table III.

Table III

Agg'utinogens determined by the gene	Hr antigen Present (+) Absent (-)	Genotype Frequencies (Caucasian race)
Rh'	(-)	1.0 per cent
Rh ₁	(-)	54.0 per cent
rh	(+)	13.0 per cent
Rh ₂	(+)	15.0 per cent
Rh ₀	(+)	2.0 per cent

Occurrence of the Hr antigen as related to the Rh factor.

3. IMPORTANCE OF THE RH FACTOR

a. Transfusion Reactions

The role of the Rh factor in blood transfusions is second only to the A-B-O factors in the production of transfusion reactions. Reactions resulting from the use of Rh incompatible blood can only occur when the recipient has been previously sensitized to the Rh antigen present in the donor's red blood cells since there are no normal Rh antibodies in human blood. Careful Rh determinations and proper use of whole blood not only eliminates the possibility of immediate transfusion reaction, but also protects the Rh negative recipient from becoming sensitized to the Rh factor. This is of special importance in females of reproductive or younger age, since it reduces the possibility of their having erythroblastosis future offspring.

Rh typing for blood transfusion is based on the principle that Rh positive blood can be given only to Rh positive recipients while Rh negative blood can be given to both Rh positive and Rh negative recipients. Since the Rh₀ (D) antigen is the most antigenic as well as being present in 85% of the Caucasian race, Anti Rh₀ serum is used to classify both donors' and recipients' blood. Bloods determined to be Rh negative with 85 per cent anti-serum include all true Rh negatives as well as a few bloods containing the weaker Rh' and Rh'' antigens. Using this method of typing no true Rh negative recipient will receive the highly antigenic Rh₀ agglutinin, but may occasionally receive the weaker Rh' and Rh'' agglutinogens. The use of 87 per cent anti serum (anti Rh' and Rh₀) on the donors' blood further eliminates the

possibility of the Rh negative recipient's receiving the Rh' antigen, since all blood classified Rh negative with the 87 per cent serum will be true Rh negatives with the exception of less than one per cent of bloods which will have the weak Rh'' agglutinin.

TABLE IV

Rh Antigen Landsteiner-Fisher		85% serum agglutinates	87% serum agglutinates	genotype incidence
rh(neg)	cde	(—)	(—)	13.0%
Rh'	Cde	(—)	(+)	1.0%
Rh''	cdE	(—)	(—)	0.5%
Rh'Rh''	CdE	(—)	(+)	.01%
Rh ₁	cDe	(+)	(+)	2.0%
Rh ₂	CDe	(+)	(+)	54.0%
Rh ₀	cDE	(+)	(+)	15.0%
Rhz	CDE	(+)	(+)	14.5%

Reaction of Rh antigen with 85 per cent (anti D) anti-serum and 87 per cent (anti C and anti D) anti-serum.

Unfortunately, Rh antiserum as produced commercially is not entirely reliable, for positives using one company's product may be negative to the comparable antiserum of another company. Standardization of antiserum is poor and inconsistent, consequently all Rh typing should be accepted with reservation and rechecked whenever indicated.

As has been shown, it has become standard procedure to use Rh negative blood indiscriminately for Rh positive recipients. Theoretically, the Rh negative donor's blood is strongly Hr positive, while the Rh positive recipient's blood is conceivably Hr negative. Sensitization to the Hr antigen in the Hr negative individual is inevitable under such circumstances and is beginning to be reported in the literature as the cause of transfusion reactions.

b. Production of Erythroblastosis Fetalis

The disease, erythroblastosis fetalis, cannot be divorced from the production of transfusion reactions by Rh factor incompatibilities, since each is a manifestation of the same antigen-antibody reaction. Frequently, the pregnant Rh negative female has been previously sensitized to the Rh antigen by indiscriminate transfusion with Rh positive blood for some illness totally unrelated to the existing pregnancy. As this might indicate, the production of erythroblastosis fetalis is directly related to the degree of Rh sensitivity of the mother.

The Rh negative female who is pregnant with an Rh positive fetus may become sensitized by

fetal agglutinogens which escape thru the placental barrier. The antibodies thus produced in the mother's circulation pass freely thru the placental barrier and agglutinate the fetal red blood cells. The effect is the same whether the antibodies result from indiscriminate blood transfusion or pregnancy. It was thought originally that the anoxia produced by the profound anemia damaged the liver, the capillaries, and the brain causing hypoproteinemia, severe hydrops, and kernicterus. Recent investigation indicates that Rh antigen is found in liver, spleen, and lymph tissue as well as the red blood cells. Each tissue may serve as the primary shock organ of the antigen-antibody reaction rather than damage occurring secondary to anemia. In either event, the fetus may suffer from hemolytic anemia of the newborn, icterus gravis of the newborn or fetal hydrops, according to the severity of the reaction. The degree of fetal disease, however, is not necessarily proportionate to the amount of maternal sensitivity indicated by Rh antibody titers. High antibody titers showing marked increase during pregnancy may be caused by a non specific antigen, the "anamnes-tic effect", while the fetus is Rh negative and unaffected by the antibodies. A severely dis-eased fetus may, conversely, result from in-complete or blocking antibodies which are not demonstrable by ordinary saline titration.

c. The Rh Factor and Disputed Parentage

The Rh genotype of all parties directly in-volved in cases of disputed parentage is of un-deniable value. In response to many requests by legal authorities, Wiener has compiled some rather complex but interesting tables from which it is possible to make certain predictions re-garding the consequences of matings of the vari-ous Rh genotypes. Table V is a representative portion of one of these tables and demonstrates their scope.

TABLE V

Mating	Parentage poss. if child is	Parentage excluded if child is	Parentage improb- able if child is
rhXRh"	rh' & Rh"	Rh ₁ , Rh ₀ , Rhz, Rh ₀ , Rh', and Rh"	
rhX Rh/Rh"	Rh' & Rh"	Rh ₁ , Rh ₀ , Rhz, and Rh ₀	Rh'Rh" and rh

Taken from Wiener (16), Table III.

4. PREVENTION OF DISEASES RESULTING FROM RH ANTIGEN-ANTIBODY REAC-TIONS

a. Prevention of Transfusion Reactions

There is no substitute therapy for prevention of transfusion reactions caused by Rh antigen-antibody combination. Primarily a problem of Rh antigen typing, which has already been dis-cussed, the reaction can be completely elim-inated by intelligent use of the information thus obtained.

Although transfusion reactions caused by Rh factor incompatibilities may be entirely elim-inated by proper Rh typing, a new and related problem is gaining substance, i.e. Hr transfusion reactions produced indirectly from promiscuous use of Rh negative blood on Rh positive indi-viduals. As with the Rh factor, this problem can be eliminated by Hr antigen typing. Un-fortunately, Hr typing sera are not readily avail-able at the present time making routine Hr determinations impractical.

b. Prevention of Erythroblastosis Fetalis

Prevention of erythroblastosis fetalis is direct-ed toward the Rh sensitivity of the mother prior to parturition and follows through the infant in the neonatal period. The disease oc-curs only about once in forty deliveries where the mother is Rh negative and the father is Rh positive. Because of the relative infrequency with which the disease occurs when these opti-mum conditions exist for it, it has become the policy to anticipate it only when Rh sensitivity is present before the pregnancy was begun. Careful Rh typing should be a part of pre natal care, however. When it is found that the mother is Rh negative it is important that the husband's Rh type be determined. In the event he is Rh positive, the possibility of an erythroblastotic in-fant must be considered. With the first or second pregnancy and in the absence of a his-tory of previous blood transfusions, it is rela-tively safe to do nothing more than observe the patient closely throughout the pregnancy. However, if there is reason to suspect that Rh sensitivity is pre-existant, more strict measures are necessary. Rh antibody titres must be taken early in the pregnancy and repeated as fre-quently as necessary to determine the degree and rate of alteration of concentration of mater-nal antibodies.

Increase in magnitude as well as rate of change are the two most reliable indicators of the presence of erythroblastosis fetalis. Unfor-tunately, a certain amount of fluctuation of antibody titre is inherent in the modes of anti-

body measurement and it is often difficult to duplicate titre values on the same specimen. When properly standardized, however, the normal antibody titre should not vary by more than one dilution tube, i.e. 1/16 to 1/32. A titre on a subsequent determination of 1/64 would be considered a significant elevation of Rh antibody concentration.

In addition to testing for increasing amounts of the "blocking" antibodies, it is important to test for Rh antibodies in both saline and albumin suspensions. It is thought that an increase in saline antibodies denotes a less severe prognosis than does an increase in albumin antibodies.

As has been stated previously, the maternal Rh antibody concentration may rise when the fetus is Rh negative. In this case the antibodies could have no damaging affect upon the fetus. This situation may arise when the father is heterozygously Rh positive and capable of producing both Rh positive and Rh negative offspring. It is, therefore, of considerable prognostic value to know whether the father is Heterozygous or Homozygous, and this should be determined whenever possible. Determination of Rh type of the other children may provide the desired information.

Efforts to reduce the concentration of maternal Rh antibodies have been relatively unsuccessful. Repeated partial blood replacement transfusions were found to produce little reduction in antibody titre. This was apparently due to the fact that the antibodies are present in the maternal tissue as well as in the circulation. Haptenes, which Landsteiner defines as a specific protein free substance which combines with antibodies but has no antigenic affect, have been infused in large quantities without appreciable benefit. Unger reports that frequent injections of Typhoid or Pertussis vaccine may reduce maternal antibody concentrations by competing with the Rh antigen in antibody production. However, this method is still under investigation.

Since fetal protection from maternal antibodies

cannot successfully be provided as indicated, interruption of the pregnancy is thought to be a method of removing the fetus from their influence before significant damage is done. Unfortunately, it is difficult to diagnose erythroblastosis fetalis antepartum and there is a definite risk of obtaining a premature non-erythroblastic infant. It must be remembered also that prematurity is a disease not without hazard, and when added to erythroblastosis fetalis further reduces the infant's chance of survival.

Although there is no available specific quantitative test for the presence of erythroblastosis in the newborn, the Coombs (direct developing) test is of definite prognostic value. It is important that the test be performed on blood taken at the time of delivery, usually on a sample taken from the umbilical cord. The extent of the value of the Coombs test is illustrated in Table VI.

Severe erythroblastosis fetalis has been treated with some success by replacement transfusions in the immediate neo-natal period. The object being to replace the fetal blood with blood whose serum is void of Rh antibodies and whose cells will not react with Rh antibodies which might remain, thus terminating the disease producing antigen-antibody reaction. In addition, this therapy provides an adequate oxygen carrying mechanism to replace that destroyed by the disease. The continuous transfusion and coordinated withdrawal method leaves approximately 36.7 percent of the original 250cc of infant's blood. The method of intermittent withdrawal of 50 cc of infant's blood and injection of 50 cc of Rh negative blood repeated five times removes about 75 per cent of the original 250 cc of infant's blood.

5. SUMMARY

The theories of inheritance and nomenclature as proposed by Landsteiner and Wiener are compared with those proposed by Fisher and Race and the basic differences and similarities noted. The importance of Rh antigen-antibody reaction in the production of Transfusion Reac-

TABLE VI

Coombs Test Reaction	Severity of Erythroblastosis Fetalis
Negative	Rh sensitized Red Blood Cells not present
Positive (weak)	Sub-clinical to mild erythroblastosis fetalis
Positive (strong)	Moderate to severe erythroblastosis fetalis including fetal hydrops

Significance of negative or positive Coombs test performed on newborns blood.

tions and Erythroblastosis Fetalis is discussed as well as the role of Rh genotype in cases of disputed parentage. Finally, current trends in therapy of disease resulting from Rh antigen-antibody reaction are evaluated.

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PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL HOSPITAL CASE NO. 29112

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

First admission: A fifty-two-year-old single, former fisherman entered the hospital because of persistent burning, epigastric pain.

Approximately twenty-five years before admission the patient began to suffer with occasional attacks of persistent burning epigastric pain, which was usually relieved by soda or food. These attacks occurred many times each year and lasted about a week but never interfered with his daily activities. Occasionally during an attack he belched a great deal, but he did not vomit. Seven years before entry, following the death of his mother, he was forced to live alone. Since then the attacks had occurred more often. A year before admission the pain became severer, and the patient gradually lost a great deal of weight and felt weak. He was seen in the Out Patient Department. At that time a healed, nonobstructing duodenal ulcer was demonstrated by x-ray studies. Ulcer diets partially relieved the discomfort, but the patient failed to gain weight.

The family history was noncontributory.

When thirty-two years old the patient had a sore on the glans penis, which healed promptly following topical treatment. Six years later both

lower legs were amputated at the calf because of gangrene of the feet following frostbite.

Physical examination disclosed a markedly emaciated man who was nothing more than "skin and bones". However, he appeared to be comfortable. Examination of the heart, lungs and abdomen was negative.

The blood pressure was 88 systolic, 64 diastolic.

The examination of the blood revealed a red-cell count of 5,290,000 with a hemoglobin of 90 per cent, and a white-cell count of 7400 with 82 per cent polymorphonuclear leukocytes. The urine was normal. The blood Hinton test was negative. A stool was guaiac negative. A barium meal demonstrated a characteristic clover-leaf deformity in the duodenal cap but no crater was visible; the pylorus opened readily. A barium enema was negative.

The patient improved and gained weight on a high-vitamin, high-calory diet with supplementary iron, and was discharged on the thirty-third hospital day.

Final admission (six years later): The patient was readmitted because of sharp, crampy abdominal pain and constipation.

Following discharge the patient again suffered with epigastric burning pain, weakness and weight loss despite an adequate diet and rest in a convalescent home. Three and a half years later he began to worry about "people talking about him," and his abdominal pain seemed worse. Occasionally he became bloated and had slight heartburn when he ate small amounts of food. He never became distended and did not belch, but passed large amounts of flatus, which seemed to relieve him. Six months later a barium meal demonstrated that the duodenal cap was grossly deformed and that there was a

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Colonic Tenderness . . .

Diarrhea,
Short Attacks . . .

Constipation . . .

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—Selesnick, S.: *The Treatment of Amebiasis*, Connecticut M. J. 12:946 (Oct.) 1948.

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RESEARCH IN THE SERVICE OF MEDICINE **SEARLE**

shallow ulcer crater posteriorly; there was also some associated spasm of the first portion of the duodenum. The remainder of the examination was negative, as was a barium enema. The patient was treated with tincture of belladonna and a six-meal-a-day diet and seemed to improve. A gastrointestinal series four months later showed no definite evidence of activity in the crater of the duodenum.

Four days before entry he began to suffer with rather severe generalized abdominal cramps, which were most marked in the upper quadrants and were not relieved by food. These continued to the time of admission. He did not feel nauseated and did not vomit. Since the onset he had not moved his bowels or passed any gas, despite a desire to do both.

Physical examination revealed a mildly disoriented man. Examination of the heart and lungs was negative. The abdomen was moderately distended. There were generalized spasm and tenderness, but these were most marked over the lower abdomen. One observer demonstrated shifting dullness in the flank. The rectum was filled with firm impacted feces. The prostate was twice its normal size, and was moderately tender and firm. No pelvic masses were felt, and no areas of tenderness were elicited.

The blood pressure was 72 systolic and 40 diastolic.

The red-cell count was 3,350,000, and the white-cell count 3500. The urine showed a three plus test for albumin.

A flat x-ray film of the abdomen showed marked dilatation of the sigmoid and a ground-glass appearance suggestive of free fluid. A small amount of barium inserted through the rectum passed to the rectosigmoid, where it appeared to be blocked; it was difficult to be certain of this, however, because the patient's relaxed anal sphincter permitted spilling of the barium.

Despite the administration of infusions of physiologic salt solution and glucose, blood transfusion and oxygen, the patient failed rapidly and died approximately sixteen hours after admission.

DR. FRANK J. MILLOY

The diagnosis of this case today is so obvious—that I am most fearful of the Pathologist's report. But feeling rather certain that Dr. Bank has no ulterior motives, I shall proceed with the

obvious. This 58 year old man suffered from a duodenal ulcer for at least 31 years. There is no argument any more quite so ridiculous as the old one about the best treatment for peptic ulcer, because it is generally admitted now that 9 out of 10 or 19 out of 20—or possibly more—ulcers heal spontaneously without any medical treatment. But now and again there is an occasional ulcer that needs real treatment—whether medical or surgical and the results are excellent—and patients are saved years of suffering. According to the history—the x-ray at the time of the first admission showed the characteristic clover-leaf deformity of duodenal ulcer—but not visible crater. Apparently the barium meal emptied in normal time. But this does not mean that food left the stomach in the normal time. It is more than likely that if this man has been on accurate ulcer treatment with enough alkali to control his acidity—and his stomach emptied out at night by stomach tube—or if he had had the classic posterior gastro-enterostomy that he would have been saved years of suffering and would have avoided the accident which caused his untimely death. It would seem that this man's ulcer continued to progress and resulted in pyloric obstruction—benign in type—until his diet was reduced and reduced—and he finally starved down to the point where he was described as nothing more than "skin and bones". He reached the point where he became anemic and his red cells dropped to 3,350,000.

Then four days before the final entry something happened. He began to have severe crampy, generalized abdominal pains, but most marked in the upper quadrants. These pains continued for 4 days and his bowels did not move and he did not pass gas. There was generalized tenderness and spasm of the abdomen, but most marked over the lower part. There was shifting dullness in the flank. He was in shock with a blood pressure of 72 over 40. The obvious conclusion is a perforated ulcer. And by this time—after 4 days he had generalized peritonitis. There was free fluid in the abdomen. The only finding out of line with the generalized peritonitis is the low white count of 3500. But the man had a severe secondary anemia to start with and this included the low white count—and this peritonitis is more chemical than infectious from the acid contents of the stomach, so there was no white count response. The flat x-ray showed marked dilatation

of the sigmoid—this is the usual location of the beginning point of the chemical peritonitis—as the free fluid gravitated into the lower flanks—I wonder why the x-ray did not show free air below the diaphragm. Probably we should see the films but maybe it was taken with the patient flat on the table.

With the historian minimizing the evidence of active peptic ulcer—and with the obstruction to the barium enema in the recto-sigmoid area one might be misled by assuming that there was an obstructive lesion in the lower colon, most likely a malignancy. But I think this is unlikely. The obstruction in this colon was due to paralytic ileus produced by the peritonitis. The patient died of general peritonitis and shock following the perforation of a peptic ulcer.

DIFFERENTIAL DIAGNOSIS

Dr. Edward B. Benedict: This is a fairly obvious history of duodenal ulcer—epigastric pain relieved by food—and x-ray examinations on several occasions confirmed the diagnosis.

The sore on the glans penis is probably of no importance. It healed promptly, and later a Hinton test was negative. I cannot relate that to the gastro-intestinal story.

The fact that he was down to “skin and bones” on the first admission makes one think of carcinoma, but since he recovered so rapidly and since his red-cell count was normal, such a diagnosis seems unlikely. Furthermore, the patient was alive six years later.

Barium enemas were done several times and were consistently negative until the last admission, which may be of some significance.

The interesting part of the story is the acute episode that began four days before the final admission. The symptoms were then characterized by severe generalized cramps, mostly in the upper quadrants, and the patient had not moved his bowels or passed any gas. The question is whether he had a large bowel obstruction with perforation or a perforated duodenal ulcer. Against a perforated duodenal ulcer is the fact that he had no sudden pain, as one would expect with a perforated ulcer, and there is no mention of any air under the diaphragm in the flat plate. He had an anemia, which would not be explained by a perforated ulcer, and a barium enema would probably not have been given if his attending physicians had thought the lesion was an acute perforated ulcer. The anemia certainly goes with a carcinoma of the sigmoid,

and the x-ray findings were consistent with a perforated carcinoma of the sigmoid. The white-cell count was low and cannot be explained by perforation unless the patient had an overwhelming infection, with no white-cell response. The temperature, pulse and respirations are not given.

From what I have read so far I am inclined to diagnose a duodenal ulcer and, in addition, a perforated carcinoma of the sigmoid. Will you show the x-ray films, Dr. Holmes?

Dr. George W. Holmes: Most of the x-ray films were taken at previous admissions. There is only one film taken at the last admission, and I am afraid that it is not going to help us. Apparently no film was taken at the time he spilled the enema. The films taken two years before the final admission were interpreted as negative, and I see no good reason to think differently. The only possibility is in the region of the cecum, but there is a good mucosal pattern all the way through and I am inclined to agree with the report. Of course there was plenty of time for something to have happened in the interval. In the last film there is a loop of dilated bowel on the left side, which appears to be large bowel. The bowel above it looks as if it contained fecal material. In other words, there is evidence of obstruction rather low in the large bowel, and nothing more.

Dr. Benedict: How much weight do you put on the fact that the patient expelled an enema?

Dr. Holmes: If he had obstruction low down and was rather sick that is not an uncommon happening.

Dr. Benedict: You think that he probably had obstruction?

Dr. Holmes: Yes. The only other explanation is that he was too sick to pay attention to what was going on.

Dr. Benedict: I shall stick to my diagnosis.

Dr. Tracy B. Mallory: In view of the profound malnutrition, I doubt that the anemia was significant.

A Physician: Was there any spinal-fluid test to rule out neurosyphilis?

Dr. Mallory: No. The opinion of the service was approximately that of Dr. Benedict. It was believed that the patient had large-bowel obstruction and that the duodenal ulcer was inactive.

CLINICAL DIAGNOSES

Volvulus of sigmoid, with perforation and peritonitis.

Perforated duodenal ulcer?

DR. BENEDICT'S DIAGNOSES

Duodenal ulcer.

Carcinoma of sigmoid, with perforation.

Peritonitis, general.

ANATOMICAL DIAGNOSES

Duodenal ulcer, with perforation.

Peritonitis, generalized.

Tuberculosis, healed, right apex.

Arteriosclerosis, generalized.

Amputation of both lower legs.

PATHOLOGICAL DISCUSSION

Dr. Mallory: At autopsy we found a perforation, 0.5 cm. in diameter, of the duodenum through the base of a chronic ulcer. The large bowel was obstructed, but merely by fecal impaction, which was of impressive extent. There was, of course, a generalized peritonitis. Nothing else of significance was found. There was no evidence that he had ever had syphilis.

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

Editorial

GENERAL McARTHUR

No group in our nation is more affected by war or peace than the Medical Profession. So no group listened more intently to every word uttered by General McArthur on his return home. And in as much as so many members of the profession served in the South Pacific theatre in World War II very definite opinions have been formed. It goes without saying that General McArthur is one of the great personalities of this era. And great personalities are invariably both loved and hated. And from the opinions expressed by those who served in the South Pacific area General McArthur is no exception to that rule.

But there was probably not a dissenting voice on one statement uttered by the General in his San Francisco speech, from those who served in the Pacific area, or any other area and that was when he said, quote "It is wonderful to be home", unquote. The General uttered other words also since his return which are no longer passed over as 'fears of alarmists' when he stated that the Communists were the Public Enemy No. 1 of the entire free world. The American Medical Association can do a little pointing to with pride that it was one of the first large organization in this country to declare war on the Communists within our shores. For the benefit of the many men who have entered the profession in the past ten or fifteen years, when the New Deal moved into Washington in the early thirties we began to hear about socialized medicine. The leaders of the Association became aroused and in an effort to combat this menace the ill-fated National Physicians Committee was organized about 1939. This Committee began delving around in Washington and soon pointed its finger at the Federal Security Administration as a bureau packed with fellow travelers,

and the spot from whence the socialistic laws and propaganda was emanating from, the most notable being the first Wagner-Murray-Dingall bill.

Only a limited number of representatives of the profession attended the meetings of the National Physicians Committee and upon returning home tried to arouse local societies of what was going on in Washington. Much of this fell on deaf ears. Many members of the profession were in the armed services at this time and did not have a chance to realize what was occurring at home.

As the great expose of Communists in our midst is being unwound at the present time, it must be of considerable satisfaction now to those pioneers in the profession who gave their time and money in the early years of this ensuing struggle, and to possibly see some glimmer of hope that truth and freedom may still survive.

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ANNUAL MEETING REPORT

The Sixtieth Annual Meeting of the Arizona Medical Association, which was held in Tucson April 29 through May 2, 1951, very possibly will be recorded as one of the most successful Annual Meetings in the history of the Association. Much of the credit for the success of the meeting must go to our President-elect of last year, Dr. Harry T. Southworth, who, as Chairman of the Committee on Scientific Assembly, arranged the program of the scientific sessions.

Dr. John Van Prohaska of Chicago and Dr. Otto Steinbrocker of New York City were guest orators of the Association, while Dr. Conrad J. Baumgartner of Los Angeles, Dr. John S. Chapman of Dallas, Dr. Edmund L. Keeney of San Diego, Dr. Donald L. Paulson of Dallas, Dr. Kenneth Charles Sawyer of Denver, and Dr. Edward B. Tuohy of Washington, D.C., guests of the Special Society groups, also participated in the presentation of papers during the scientific sessions; as did likewise Drs. DeWitt W. Englund, Dermont W. Melick, James M. Ovens, Paul L. Singer and Marcy L. Sussman, all of Phoenix, and Drs. Lindsay E. Beaton, Hiram D. Cochran, John S. Mikell, Hugh C. Thompson and Herbert D. Welsh, all of Tucson, members of this Association.

The Special Society meetings have developed into one of the outstanding sections of the Annual Meeting. The Chairmen of the various So-

cieties exercised unusual acumen in the selection of their guest speakers.

The House of Delegates held two meetings according to schedule, and its business was transacted in record time. This result to a considerable extent can be attributed to the previous action of the House during its 1950 meeting requiring that all Reports of the Association's Officers and Chairmen of all Boards and Committees be filed in advance, and the Secretary delegated to have copies prepared and forwarded to the members of the House of Delegates, Council, and Secretaries of the component County Societies at least 30 days prior to the Annual Meeting. Reducing to resolution form all matters proposed for introduction likewise contributed much to the orderly processing of the business before the House. The following Officers were duly and unanimously elected:

- President-elect... Thomas H. Bate, M.D., Phoenix
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While the entertainment was well arranged, the golf tournament was somewhat disrupted due to inclement weather. It was necessary to extend it over the period of most of the meeting on a schedule "weather permitting." Despite this handicap, the tournament was well attended. Dr. E. Payne Palmer, Jr. of Phoenix scored a low gross of 74 and Dr. M. W. Phillips of Prescott a low net of 69. Prizes were donated through the courtesy of Martin Drug Co. and Standard Surgical Supply Co., both of Tucson, and the Association.

The social hour held at the Tucson Country Club on Sunday afternoon was a very pleasant affair; likewise the social hour and the President's Dinner Dance held on Tuesday evening, climaxing the entertainment program. An excellent steak dinner was served, during which the incoming President, Dr. Southworth, officiated with distinction, introducing the guests and officers of the Association at the head table and conferring upon Dr. Clarence Gunter in absentia the honorary degree of membership in the Fifty Year Club, recognizing outstanding service during his first 50 years of medical practice. The

musical strains of Arnie Serbin and his Orchestra held the gathering until after midnight, concluding an evening long to be remembered.

Press coverage was exceptionally good this year, for which the Association is grateful to the Tucson Newspapers and particularly to Robert Moore, also representing the Associated Press. Through the cooperation of the guest orators we were able to obtain copies of their papers in advance of the meeting, which was of immeasurable assistance in making adequate press coverage possible.

The Woman's Auxiliary, through the able Chairmanship of Mrs. Leo J. Kent and Mrs. Joseph M. Kinkade, are to be commended for their gracious assistance in caring for floral decorations at the President's Dinner Dance and as hosts to our guests, which I am sure made their visit a memorable one.

To the Pioneer Hotel staff we extend our appreciation and thanks for splendid, courteous service and outstanding cooperation throughout our visit, contributing in no small measure to the success of this our Sixtieth Annual Meeting.

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 Herbert E. Schmitz, M.D., Prof. and Chairman of Dept. of Obstetrics and Gynecology, Stritch School of Medicine, Loyola Univ., Chicago.
 Cyrus C. Sturgis, M.D., Prof. of Internal Medicine, Univ. of Michigan, Ann Arbor.
 Wm. B. Wartman, M.D., Prof. of Pathology, Northwestern University Medical School, Chicago.

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TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER, M.D.

Terramycin has joined chloramphenicol and aureomycin as effective drugs in ACUTE BRUCELLOSIS. . . . All three clear the fever rapidly act only a bit slower on the symptoms. Aureomycin is least well tolerated, due to intestinal toxicity; chloromycetin causes stomatitis in long or large dosage; and terramycin is best tolerated. . . . The relapse rate is high, about 70 per cent for all drugs, and no way has yet been found to avoid it.

The Ohio State Medical Journal says,—

1. Yandell Henderson, the Yale expert on body chemistry, has recently studied the use of HYPNOTICS IN LABOR. . . . He bars the use of all morphine drugs and derivatives.

2. In reducing SODIUM from the intake of a patient with heart failure, don't forget to use distilled water, to exclude ice-cream as well as milk, and to carefully consider drugs which may contain sodium. . . . The usual level of sodium for man (and the apes!) is 100 mg. per 1000 calories of food

3. CARCINOMA OF THE LUNGS is rare in a male non-smoker (But so is a male non-smoker).

The ancient and honorable University of Pennsylvania Medical School (No. 1 in the United States) has joined the University of Wisconsin and Kansas in the use of a PRECEPTOR PLAN for amplifying the education of medical students. . . . Students are assigned to approved groups of physicians for the summer vacation after their third year. . . . The preceptors have faculty status and (contrary to the plan in Wis. and Kans.) are scattered as far south as Florida and as far west as Montana. It could be quite a vacation.

SPONTANEOUS PNEUMOTHORAX is seen so rarely, even by chest specialists, that one might think it occurred once in thousands. . . . An Army induction center reports, however, that one in every 500 gave a history of having had such a collapse.

BRIEFS FROM THE X-RAY DEPARTMENT,—

1. A simple and efficient instrument for measuring stray radiation is the 'Minometer', about the size of a fountain pen, which may be carried in the pocket. . . . It consists of a small string electrometer and a small ionization chamber. It helps warn and protect the personnel members.

2. A LUMINOUS PLASTER TUMBLER is useful for serving barium in the dark-room. The patient can see what he is to do, and the radiologist can see that he does it. . . . It may also be

used in the hospital or at home for night use at the bedside, tho a paper cup insert is necessary.

A shopping column in one of the hospital magazines describes a couple of oddly named products. An absorbent gown is called the "Nittgown". A harness which allows a mother to carry her child while doing housework is called a "MoMper" . . . Anyone who can top these is welcome to try, but elsewhere.

Sometimes a clinical condition suggests that we look for silent sequellae; sometimes the sequellae turn up first, and force us to back-track. A URINARY CALCULUS seems to be such a sequella. . . . Several factors lead to the formation of all types of stones,—urinary stasis, vitamin A deficiency, urinary tract infections, disorders of calcium and magnesium metabolism, citric acid excretion, and production of the estrogenic hormone. . . . Two variables may also be important,—the concentration of stone-forming crystalloids in the urine, and the PH of the urine. If a crystalloid (such as calcium) is present in excess (due to such things as hyperparathyroidism, high calcium intake, an acid-ash-diet, large doses of vitamin D, the use of ammonium chloride, etc.) and the PH is shifted (to the alkaline side for most calcium stones), precipitation may occur. . . . Uric acid and cystine stone are formed in acid urine, but are uncommon.

HEPATOMA seems much more rare than it actually is. It accounts for 2% of all American malignant growths. It is often unsuspected. Four per cent of patients with portal cirrhosis die of hepatoma.

The question of which drug to use against BARBITURATE INTOXICATION is solved by Billow of New York in the American Practitioner): he combines two of them. . . . Picrotoxin is given repeatedly intravenously and Benzedrine repeatedly intramuscularly. . . . The adjuvant routine includes 1. penicillin in slowly absorbed doses; 2. maintenance of an open airway; 3. changing of the patient's position; 4. glucose (5%) in saline intravenously

Drs. Hench and Kendall of the Mayo Clinic have had a friendly competition in fan-mail as a result of their adrenal cortex work. . . . Each received a letter stating that the correspondent had written because he had chosen Dr. Hench/Dr. Kendall from a group picture in LIFE Magazine as the one who appeared most intelligent. . . .

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INTERNAL
MEDICINE
and
NERVOUS
DISORDERS

PASADENA, CALIFORNIA

They were surprised to find that the letters were by different people—but both undoubtedly intelligent!

A research project of the U. S. Army, conducted at the University of Pennsylvania, has turned out a NEW DYE FOR THE STAINING OF SKIN FUNGI. . . . It is said to be simple and specific in a field which was previously quite barren. It helps in the differential diagnosis of neoplasms, tuberculosis, syphilis, and fungus infections, and is most helpful in ringworm. . . . The point of attack is the presence of cellulose in the fungus cell. The Hotchkiss-McManus stain for cellulose and carbohydrate is used, with a basic fuchsin to give the final magenta coloring.

When THIS OSLER was a resident in medicine, he used to fear that he would miss the diagnosis of early pernicious anemia, cirrhosis of the liver, or poliomyelitis. A MORE FAMOUS OSLER used to warn people to rule out tuberculosis, syphilis, and typhoid. . . . Recently it seemed that a good method of self-analysis should include a listing of cases for the previous year which had seemed to be failures, in some part due to the physician. It is interesting to see how far the ten cases deviate from the two Osler lists,—1. A man with an acute lesion of the lung. Died. Wife wouldn't believe the diagnosis of gangrene, and that it was untreatable. 2. A case of colitis, with protracted fever. Surgeon made the unsuspected diagnosis of amebic abscess of the liver at exploratory operation. 3. Emphysema with cor pulmonale. The patient shifted to another physician because of lack of progress (and confidence). Lost ground. 4. Three children with rheumatic fever. Couldn't manage the parents nor obtain rest for the children. 5. Boy with cardiac signs of residual rheumatic activity. Schoolmaster insisted on changing to an M.D. who 'worried' less. 6. A doctor with asthma. The identity of the major and psychogenic cause was missed when he was not frank. 7. A woman scholar, diagnosed wrongly as a case of 'acute rheumatism'. She was malingerer to avoid a social guilt. 8. A spoiled rich woman needed medical observation, but was transferred to another physician because of an incompatibility. 9. A ranch guest with grippe. Refused to believe that there was not a specific cure for it. 10. A woman with an intestinal neurosis, shopping for a diagnosis. Refused to take her case. . . . CONCLUSIONS,—The cause of failure does not often seem to lie in diagnosis (providing that a lot of other cases were not forgotten). The causes did not resemble either of the Osler lists. The difficulty often seemed to be concerned either with the personality of the patient or that of the physician. . . . Dr. George Saslow of St. Louis says (in "Minnesota Medicine") "Apparently it is extremely difficult for people (with certain diseases) to sustain a co-operative relationship with

medical persons or a medical team". . . . We feel better now, but could probably try harder.



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ANNUAL REPORT OF THE SECRETARY

Having rounded the bend and in full stride hurrying down the home stretch to the goal of completion of another fiscal year of operation and the 60th Annual Meeting of this Association, it is well to pause for a moment in reflection. Too frequently in our busy lives we are all prone to accept progress as a matter of fact giving little thought to our labors and accomplishments. We have come a long way since the organization of our Association back in 1892 and many of us have seen our membership steadily grow along with the times and development of our great State and at this writing report a total of 625 among our 14 constituent county medical societies. Along with growth comes increased responsibility as well as broader opportunity.

During the fiscal year just ended three important Council Meetings were held in Phoenix each of a full day duration on June 22, 1950, July 30, 1950, and January 21, 1951. While these meetings are always well attended, bearing in mind membership is recruited from all quarters of the State, this year we have established somewhat of a record reporting full attendance at the latter meeting. Problems of vital concern to the medical profession were discussed and decisions reached which will no doubt be the subject of report of the Chairman of Council.

The Professional Board met in Tucson September 10, 1950, and again in Phoenix February 25, 1951; the Public Relations Board in Phoenix October 28, 1950; the Grievance Committee organized in Phoenix January 7, 1951, and met again on March 18, 1951; the Civil Defense and Procurement & Assignment Committees in joint session in Phoenix August 20, 1950; and the Arizona Advisory Committee to the Selective Service System (an outgrowth of our Procurement & Assignment Committee) has been extremely active throughout this fiscal year. Many of the other standing committees have likewise been active throughout the year including medical defense and especially legislation with the 20th Legislature in its first session; however, I will not attempt to outline the many problems coming before these bodies to save repetition as unquestionably each will submit their individual reports. Throughout the year I have endeavored to keep the membership informed through periodic reporting in the Arizona Medicine Journal

and the Secretaries of each of the County Medical Societies have been furnished copies of the minutes of the proceedings of all Council Meetings.

This report would not be complete without a word regarding the activities of the Executive Secretary and the mounting tasks continually placed before him and his staff, presently consisting of two stenographers. To give you a complete picture of this operation would require considerably more time and space than is allotted to this brief report. Recording and transcription of all the minutes of our House, Council, Boards, and Committees are processed through the Central Office, together with the handling of all such business and directives. Such functions as Civil Defense, Procurement and Assignment, Arizona Advisory Committee to the Selective Service System, and the Grievance Committee are a few of the added responsibilities assumed this year resulting in a considerable increase in volume of work particularly as relates to the latter two operations. Legislation received top priority during the first three months of this year and special mention is made of the able advice and competent direction received from our attorney along with the cooperation of this office.

During the year our membership records have been thoroughly checked, brought up to date and are being currently so maintained, including the posting of all dues received both State and National; minute books in summary form of all proceedings established; a complete new filing system installed and a much needed dressing up of the old undertaken; new accounting procedures under the direction of the Treasurer instituted and currently maintained, not to mention the many local, state, federal and A.M.A. monthly and quarterly reports demanded and prepared; copy for the column "To Your Health" is processed through the office as is all material for the complete publication of the "Health Activities Bulletin", and improved press relations established all under the direction of the Board of Public Relations; under direction of the President-Elect and Chairman of the Scientific Assembly, handles the many details required in arranging for the Annual Meeting and exhibitors; and let us not forget the mounting telephone calls, inquiries, and mail from almost

every source country-wide received and handled through our Central Office. Every day and many evenings your Secretary and Executive Secretary spend a minimum of 15 minutes to several hours together handling the business of this Association.

The Executive Secretary attended a Hospitalization and Surgical Insurance Conference in Salt Lake City; the Annual Meeting of the American Medical Association in San Francisco; a Civil Defense Meeting in San Francisco; the Interim A.M.A. and National Education Campaign meetings in Cleveland and a National Advisory Board to the Selective Service System meeting in Washington, D. C. during the year, reports of which appeared in *Arizona Medicine* and when he has a few minutes left attends many of the local meetings of interest to the medical profession.

In conclusion may I state that from the record of this office, it is my observation that the Officers and Council of this Association have completed another year of accomplishment fully aware of the tasks which lie ahead. I have again enjoyed serving you and I wish to take this opportunity to thank each and all of you for your splendid support and cooperation throughout the year.

Frank J. Milloy, M.D. Secretary
Respectfully submitted,

ANNUAL REPORT OF THE BOARD OF PUBLIC RELATIONS

It is my pleasure to present the following report covering the activities of the Public Relations Board of The Arizona Medical Association for 1950.

Most of the objectives which were set by the Board at the beginning of last year have been realized. Probably the most important project was the expanded publication of the *Health Activities Bulletin*. This Bulletin, coming off the press every two months, is being forwarded without charge as a public service to approximately 10,000 citizens of this state. The mailing list is growing daily, and it is the hope that it may grow appreciably during the coming year through public demand. We have had a very favorable response as to the effectiveness of this Bulletin, and the Board believes that it will and should be one of our principal public relations media in the years ahead. Its potential seems unlimited, and

through proper development it should prove very effective as a liaison publication between the general public and members of this Association.

Another of the major activities of the Public Relations Board has been the publication each Sunday in the local Arizona Republic newspaper of a medical article of timely interest to the public, prepared by a member of this Association. These articles appear in the column known as **TO YOUR HEALTH**, and the cooperation of the press to this end is gratifying. It is the intention to continue this weekly publication as frequently as space is available under the difficult national emergency and subsequent newsprint shortages, with the hope that in the future these articles may be republished in booklet form to be supplied to our doctors for distribution among their patients. Much time and effort is contributed in the preparation of these articles by our Association members, and this Board is especially grateful to them for their cooperation to this end. This activity has also received commendable public acceptance.

Your Public Relations Board has been at work preparing a small pamphlet to be entitled, **"YOUR DOCTOR."** This booklet contains information as to the medical training of a Doctor of Medicine, including his college education and medical school work. It goes into some length discussing internships and licensure and portrays many of the problems that are met with in practice, and on the whole is considered a source of splendid informative material for public consumption. Considerable time has been spent on the preparation of the numerous chapters contained therein in order that the public may have full knowledge and a better understanding of the education, training and skill of the medical profession, and responsibilities it assumes in the interest of better health and protection of the public. It is expected this publication will be off the press within the month, and copies will be available to each member of the Association for distribution among his patients. Again, it is the hope that this pamphlet will be of considerable value as a public relations medium.

The Board has not carried out as extensive an informative newspaper advertising campaign as it would like to have done during the past year. This has been due to several factors. A considerable portion of the money allotted to the

Board this year was expended in the form of a loan in connection with its expanded Bulletin publication. While this money will be repaid, it has to some extent limited the activities throughout the year. Another reason for the lack of a more intensive newspaper campaign has been the somewhat divided opinion among the members of the Board and others with whom we have consulted as to its value. During the forthcoming year we will be able to work out, and will have funds available to carry out, some sort of definite public relations program through the press.

I wish at this time to briefly report on the reaction following the discontinuance of our radio participation program. Very few comments were received following the termination of contract for weekly radio broadcasting engaged in for several years past. It is surprising to note that it hardly caused a ripple when the program was discontinued. The Board now feels its action was justified. What we may do in the future regarding radio and television programs will be dependent upon the circumstances as they develop.

Now that a state-wide Grievance Committee has been definitely organized and is under way, the Board feels that it should receive some publicity and that during the coming year it should promote this phase of The Arizona Medical Association's public relations program to the fullest. In other states a limited advertising program, calling the public's attention to the facility available to them enabling presentation of their grievances for review has proved bene-

ficial.

The Public Relations Board of The Arizona Medical Association is profoundly interested in the county public relations programs. We have watched with interest the adoption of the go-ahead proposals by the Maricopa County Medical Society to institute a program similar to that of the Alameda County Plan. We are hoping that in at least the two larger County Societies, Maricopa and Pima, these plans can be put into operation. After all, a good public relations program should originate within the County Societies. The state level has a definite function to be performed, of necessity informative and educational, whereas on the county level the public relations program can reach the "grass roots" and more satisfactorily take up the problems that pertain to individuals and doctors in the everyday practice of medicine.

During the current fiscal year a sum of \$5,000 was appropriated to the Board of Public Relations for its work. The Treasurer reports that as of February 28, 1951, there has been expended a total of \$2,907.22, including the loan to Mr. McMeekin. Approximately \$1,650 of the unexpended balance is "earmarked" for the publication and distribution of the pamphlet, "YOUR DOCTOR." It is hoped that during the forthcoming year Council will see fit to allot at least \$5,000 to the public relations program. It is the considered judgment of this Board that its efforts should be continued and present projects maintained.

Respectfully submitted,

Marriner W. Merrill, M.D. Chairman.

THE ARIZONA MEDICAL ASSOCIATION, INC. PROFESSIONAL BOARD

Meeting of the Professional Board of The Arizona Medical Association, Inc., held in the Saratoga Room of Hotel Westward Ho, Phoenix, Arizona, Sunday, February 25, 1951, convened at 11:20 A.M., Dr. Arthur J. Present, Chairman, presiding.

ROLL CALL

Present: Doctors—Born, E. A., Hastings, Robert E., President; Kinkade, J. M., Present, Arthur J., Chairman; Thompson, Hugh C., and Zemsky, Boris.

Excused: Doctors—Lytton-Smith, James, Milloy, Frank J., Secretary; Snyder, B. L., Van Epps, Charles E.

Guest: Doctor—Ward, James P.

PAPAGO PARK VETERANS HOSPITAL

Dr. Ward explained the status of plans proposed to approach the Veterans Administration through the Public Health Service's Surplus Property Board to obtain the Papago Park Veterans Hospital in Phoenix, fully equipped, when vacated by the V.A. when they take over their new hospital facilities on Indian School Road and Seventh Street. It was planned on transfer of the properties comprising a 144 bed hospital to operate it as a tuberculosis sanatorium and George V. Christie, Vice-President of the State Tuberculosis Association, heading a committee as its Chairman is endeavoring to seek through the legislature an appropriation to

operate such institution. It is presently doubtful however that any progress has been made as recently it was learned that due to equipment shortages and difficulty in procuring new, the V.A. proposes to take most of their equipment with them. This will result in the need for additional funds considerably in excess of the amount originally believed adequate for operational purposes and it is doubtful now

whether the project would be feasible.

ARIZONA TAX RESEARCH ASSOCIATION PUBLIC HEALTH APPROPRIATION

Dr. Present presented a pamphlet prepared and distributed by the Arizona Tax Research Association questioning the budget appropriation figures for increased funds to be allocated to the State Department of Health now before the Legislature for consideration.

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Dr. Ward explained that their contention is a matter application of figures. The report was drafted taking into consideration total monies expended for welfare, relief and care of the indigent sick. "While we are all talking the same figures, those which I have stressed takes into account only that portion necessary in my opinion to develop an expanded and more positive preventive program," stated Dr. Ward. Steve Spear, the author of the report, is well familiar with the facts and it was questionable whether much could be gained in responding and taking issue with the presentation. The figures used included total expenditures or appropriations for county, city and state lumped together and a comparison should be made with other of the 48 states which statistics are not available. Dr. Ward's contention is and has been that while states, counties and federal government have been appropriating substantial funds for public health services, the Legislature of this State has not provided adequately in support of a preventive health program. This State's 14c per capita appropriation is approximately three times less than local and federal contributions.

REPORTING OF INFECTIOUS DISEASES

Dr. Ward stressed the need for more adequate reporting of infectious diseases and suggested that possibly the Professional Board could communicate with the physicians urging fuller co-operation. Approximately only 45% of the doctors are reporting the instances of such diseases. The Public Health Service is quite concerned over the inability to determine just what the illness rate normally is and it is desirable to establish a base line.

Criticism of the form of card content was voiced and it was suggested as a means to improve reporting that it be revised and possibly through legislative action compelling such reporting, a solution might be effected.

Dr. Ward advised that effort is being and has been made to realize such changes in co-operation with the Public Health Service who is endeavoring to standardize its statistical reporting on a world-wide basis.

It was agreed that Dr. Ward be authorized to communicate with the Public Health Service expressing the views of this Board as pertains to an improved form of report card and that he also address letters to the doctors' secretaries urging them to assist the doctor in this con-

nection and follow through closely the reporting of all infectious diseases.

PRACTICE OF PSYCHOLOGY—LICENSURE AND REGULATIONS

Referred by Council for Board consideration is the subject of licensing and certification of psychologists and adoption of regulations therefor sought by the Arizona Psychological Association.

Dr. Born reported that the problem has been handled most effectively in the State of New Jersey. It is a question of licensing and thence setting forth regulations whereby they should practice. Definitely they should not practice clinical psychology except under medical direction. New Jersey has covered this point and a copy of the plan has been applied for. Considerable discussion ensued.

It was moved by Dr. Hugh Thompson, seconded by Dr. Zemsky and unanimously carried that Dr. Born be authorized to answer the letter after he has studied the New Jersey plan for licensing and regulating the practice of psychology to his satisfaction, along lines discussed here.

ARIZONA STATE HOSPITAL

Dr. Born reported on the recent charges of Dr. Simecek relating to the operation of the Arizona State Hospital following his resignation. While it is definitely overcrowded especially since the closing of the Florence unit and transfer of its patients back to Phoenix, as far as the care of the mentally ill is concerned its program ranges favorably with others of the 48 states and has been progressively improved throughout the past several years including the problem of segregation, treatment of tuberculosis and increase of the nursing staff. The opinion was expressed that this Sub-Committee could actually serve quite a useful purpose, insofar as the public is concerned, if a periodic report issued, for press release, relating to operations and conditions at this institution.

It was moved by Dr. Hugh Thompson, seconded by Dr. Kinkade and unanimously carried that the Sub-Committee on the State Hospital or Mental Disease make up a report which would be submitted to us for approval and then given to the papers, stating the present set-up at the State Hospital and see that it hits all newspapers of the State so that the public is not either unduly scared of the institution or unduly complacent.

DIABETES DETECTION DRIVE

Dr. Present reported that last September the State and County Societies were solicited by the American Diabetes Association encouraging the institution of a Diabetes Detection Drive. Apparently from their viewpoint it is desirable to have a committee formed through the medical societies to participate in such a proposed drive. While personnel is not now available, Dr. Ward indicated that possibly at some later date the Public Health Department might be in position to undertake some sort of a screening test in conjunction with its x-ray (bus) program over a period of approximately one year.

It was directed that a letter be written to each of the Secretaries of the County Medical Societies asking their reaction as to a state-wide survey in accordance with the American Diabetes Association's annual campaign.

SEMINAR PROGRAM

Dr. Thompson reported the results of the seminar program on the Medical Aspects of Atomic Warfare undertaken and completed last fall. Drs. Donald A. Polson, Marcus W. Westervelt and Wilkins R. Manning together with Frank Williams of the State Department of Health participated. Such activity involved an expenditure of approximately \$932.11 and effort is now being made to secure reimbursement therefor from the State as a part of and in conjunction with its civil defense program. The total attendance reported was 52 physicians, 36 nurses and 49 other people, outside Maricopa and Pima Counties.

MEDICAL SCHOOL ENROLLMENT

Discussion ensued in the matter of placing prospective medical students of this state. It was pointed out that in the past effort has been successful in placing a limited number of boys in such schools as Harvard, Hopkins, Columbia, Yale, Tulane and Stanford, however it is difficult to gain admission into those schools having state affiliation such as the University of Michigan which limits out-of-state student entrance. It was suggested that effort be again made to effect legislation which would realize state aid to students in lieu of a medical school such as is in effect between Colorado and three other states.

It was moved by Dr. Hugh Thompson, seconded by Dr. Hastings and unanimously carried that this Board recommends to the Council that consideration be again given relative to the

supporting of Arizona medical students and out-of-state universities in somewhat the same manner as is being done with other states in cooperation with the University of Colorado School.

HEALTH FOUNDATION

Dr. Present reported receipt of a communication from Kurt Mathias, a Phoenix masseur who specializes in Swedish massage and is interested in establishing a state-wide health foundation. He sought the endorsement of this Association. He was advised that the inherent nature of this Association requires that its support be given to regularly approved and established hospitals, health organizations and such endeavors as represent the combined efforts of practicing members of the medical profession.

KOCH'S SERUM

Dr. Present spoke on the practice of certain doctors administering Koch's Serum to patients at fixed fees of from \$100 to \$130 per shot for treatment of cancer, contrary to the policy of A.M.A. as evidenced by numerous articles appearing in the A.M.A. Journal over the past several years, one in particular being submitted for review as it appeared in the August 27, 1949 issue under the Bureau of Investigation. It has been the concern of the Arizona Division—American Cancer Society during the past year or so.

It is the view of the Professional Board that this matter be referred to the Grievance Committee with the thought that the doctors might be called before it and admonished for taking patients in on such a nostrum.

HARD OF HEARING—ANNUAL MEETING

Dr. Kinkade reported that this will be the first year they will have a program in conjunction with the Annual Meeting of the Association. Dr. Victor Goodhill of Los Angeles, Otologist for John Tracy Clinic, will be guest speaker presenting the subject: "Deafness in Childhood." Lay participation will be encouraged and an appealing motion picture entitled: THOUSANDS SHALL HEAR will be shown.

The Hearing Center is going good in Pima County and results far exceed expectations. Maricopa County's Center under Dr. Thoeny is likewise progressing satisfactorily and organization of similar operations in other counties is the hope for the future.

VIVI-SECTION OF ANIMALS

Dr. Present offered for discussion a recent ad-

vertisement appearing in the local papers, apparently paid for by the National Anti-Vivi-Section Society. It was expressed that either this Board or Council should go on record as stating very strongly that every effort should be made throughout the Society to counter-act this perfectly maudlin publicity.

Robert Carpenter, Executive Secretary
for
Frank J. Milloy, M.D., Secretary

EXCERPTS FROM SECRETARY
LULL'S LETTER

Paper Praises Doctors' Emergency Phone System. Not too many years back, the public's most common criticism of the medical profession was based on its inability to get a doctor at night, Sundays or holidays. It was not unusual for newspapers to tell tragic stories about babies dying because a father or mother was unable to reach a doctor. The A.M.A. and state and county medical societies—in fact, everybody—led a concerted drive to correct the situation and, judging from a recent illustrated story in the New York World-Telegram, the combined efforts are paying dividends.

It was only a few weeks ago that the A.M.A.

Board of Trustees reported that as of January 1, 1951, there were 329 night and emergency call plans established and functioning as compared with 60 in the summer of 1948.

The New York World-Telegram told in detail how the Doctors' Emergency Service set up last August by the Medical Society of the County of New York operates. Five of the services are operating in New York City, with each borough having its own. In February, the emergency calls from Manhattan alone totaled 308, and Queens had 500 calls.

When the service started, the county medical society rounded up 250 doctors who agreed to answer emergency calls, some by day, others by night and still others during holidays. Sometimes the service had to call eight or 10 doctors before finding someone to go. But over the months, the New York paper said, doctors have been on their way to patients in from seven to eight minutes on the average.

The New York news story, telling how doctors solved a problem and how they now are giving their patients service in the true meaning of the word, did the profession a world of good from a public relations standpoint. The story, illustrated with a picture of a frantic mother calling for a doctor while holding a sick child in her arms, another showing a service telephone operator taking the call, and a third showing the doctor ringing the door bell of the mother's apartment, did a marvelous job of "selling" the public on the good service provided by the medical profession in a big, bustling city.

Ewing Slaps Voluntary Plans Again. In his recent annual report to Congress, Federal Security Administrator Ewing showed again his determination to prove that voluntary insurance programs have no place in the health care of the American people. He renewed his proposals for a basic national system of social insurance, with complete coverage for all gainful workers.

As the A.M.A. National Education Campaign headquarters pointed out in a letter to doctors, Mr. Ewing said on Page 12, paragraph 2, of the report: "While voluntary insurance has achieved considerable coverage, it offers only limited protection, mainly to the middle-income groups in the larger urban areas, and *cannot* effectively meet the needs of the entire population."

On Page 16, he said: "Government health insurance administered on a decentralized basis as part of a national contributory social insurance

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system offers the most adequate and economical method of guaranteeing that there will be no financial barriers to needed medical care."

All of which proves to us that Mr. Ewing is still determined, despite the wishes of the electorate in throwing out certain candidates, that he is in favor of socialized medicine.

As a whole his report painted a pretty black

picture so far as the health of the nation is concerned.

He said, for example, that children of school age have been the most neglected among all age groups in this country. His views, we know, are contrary to all health indices which show that American School children are the healthiest in the world.

TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS

Subacute bacterial endocarditis, more accurately designed as endocarditis lenta, is a slow, progressive disease in which vegetations are formed on valves and endocardium. These vegetations become organized and are followed by the production of new vegetations, so that ultimately the mass may be large, composed chiefly of vegetations and more deeply of granulation tissue and cicatrization. The micro-organisms responsible for the disease are principally those of alpha streptococci of the viridans group and gamma nonhemolytic streptococci. The cocci are readily stained in the superficial layers of the vegetations and less readily in the deeper fibrotic and calcified layers. A therapeutic agent, to be effective, must, therefore, be brought in contact with these vegetations over a long period of time in order to reach the cocci trapped in the deeper recesses of the vegetations.

The mortality of endocarditis lenta until the advent of antibiotics was almost 100 per cent. Lichtman, writing as late as 1943, states that the incidence of spontaneous recovery is about 1 per cent. Four per cent of patients treated by sulfonamides appear to recover. The combined therapy of sulfonamides and heparin and of sulfonamides and hyperthermia yielded 6.5 per cent of recoveries. The introduction of penicillin into the treatment of this disease brought about a dramatic change in outlook. Dawson and Hunter were able, in 1945, to report 15 patients cured in a group of 20. The infecting organism was *Streptococcus*. Heparin was employed as an adjuvant in most of these patients. Of five patients treated without heparin, four were cured. Gerber treated 25 patients with penicillin but without heparinization. He reported complete elimination of infection in 22 patients by more careful attention to the attainment of high blood levels of penicillin. Of 29 patients treated by him, 22 have remained well and bacteria free for six to 19 months after discharge.

Treatment with intermittent intramuscular injections of large doses of penicillin at three-hour intervals proved more effective than continuous intravenous administration of the same total daily amount. Gerber felt that the minimum duration of treatment should be five weeks. Christie, reporting on 147 patients with 81 cures, 50 fatalities and 16 patients still under treatment, emphasized that the duration of treatment was more important than the total amount given.

Bloomfield, in a recent review, emphasizes the importance of early diagnosis and of prophylactic exhibition of penicillin in connection with dental extractions and oral surgery. The question of the proper dose, he believes, can be answered only by determination of the sensitivity of the causative organism to penicillin. Intramuscular daily doses of 600,000 units of penicillin, given in two divided doses and continued for 30 days, will achieve sterilization in most patients. More resistant strains may require as much as 6,000,000 to 20,000,000 units daily.

Robbins and Tompsett state that the therapeutic effectiveness of penicillin in subacute bacterial endocarditis has resulted in the arrest of the infection in all but 10 per cent of cases. The majority of this latter group of patients are infected with streptococci of the Lancefield serologic group D, the most important members of which are commonly termed *Streptococcus fecalis* and *Streptococcus zymogenes*. These authors observed that combined penicillin and streptomycin act as coadjuvants in inhibiting growth of all the studied strains of *Enterococcus* and *Streptococcus viridans*. Six patients with persistent enterococcic bacteremia, five of whom had endocarditis, have received 6,000,000 units of penicillin and 2 Gm. of streptomycin daily. Bacteremia was promptly reversed, and there was sustained clinical improvement in all. All but one patient have been followed for periods of six to 12 months, and none has relapsed. These

uniformly good results are in striking contrast with the previous experience with the use of either drug alone in these infections and suggest that summation occurs in vivo comparable to that observed in vitro.

Fiese calls attention to the fact that, while penicillin is capable of eliminating the infection in most patients with endocarditis lenta, it will

not always prevent subsequent deterioration of cardiac function. Among the factors contributing to cardiac decompensation, he lists the previous reserve and size of the heart, the height of the temperature and the length of time before adequate treatment. Treatment with penicillin appears to postpone cardiac failure and to reduce its incidence.

WOMAN'S AUXILIARY

WOMEN OF THE YEAR



EVELYN JONES KIRMSE

Doctor's wives can be found as active members of every civic and professional organization and, as such, are performing a valuable public relation service for their husband's profession. Every year some Doctor's wife becomes outstanding in some field of endeavor and receives State and National recognition. In Arizona this year we have three women who have done this and so we nominate them our WOMEN OF THE YEAR FOR 1950-51.

EVELYN JONES KIRMSE of Whipple, Arizona was appointed by Governor Howard Pyle to serve an eight year term as a member of the Board of Regents of the University and the State Colleges. As a member of the Board of Regents, Mrs. Kirmse states that her primary interest will be "to help provide the highest aca-

demie, administrative and personnel standards in all three of our Arizona colleges and especially to interpret the needs of women students and staff members." Mrs. Kirmse is exceptionally qualified for her new appointment since she served more than a decade as dean of women at the University of Arizona and before that as teacher at Florence Union High School. She is AAUW's Status of Women Chairman. Representation of women on the Board of Regents is of particular importance in maintaining eligibility standards for University of Arizona women and in furthering the chances of the State Colleges as they seek for AAUW recognition.

MARGARET B. KOBER, Councilwoman of the City of Phoenix is the only woman member of the Charter Government, which an aroused citizenry voted into office in November 1949.



MARGARET B. KOBER

As they had campaigned for a better city government, their first act was to obtain the services of a trained and qualified City Manager. Under his guidance Phoenix has made great improvements in all departments; especially in the Public Health Department, which was reorganized under Dr. James Dolce. Phoenix was one of eleven cities receiving national recognition for proving that an interested, voting citizenry can obtain an honest, efficient government if they want it. Mrs. Kober says, "Women can help to achieve and maintain good city government by keeping the people interested and informed on all city problems and improvements. They can see that every eligible citizen votes in all elections. I have devoted much time to the study of all issues so that I may pass intelligently on City Manager suggestions. However, the magnitude of city government in all its ramifications is tremendous and to study and understand the inner workings of a city is a liberal education. Too few of us understand our government set-up on any level—city, state or national. I believe that as women we should inform ourselves and fight for good government."

CHARITY O'KEEFE THAYER started out five years ago as a leader of a small group of Bluebirds comprised of her daughter and her friends in Emerson School. When they graduated in Camp Fire Mrs. Thayer went on with them as their leader. As her interest increased her scope did also and she served as President of the Leaders Council in Phoenix. Under her regime such splendid work was done that last Fall she was signally honored by being chosen one of ten women in the United States to receive the Leaders Medallion from National Council for outstanding leadership in 1950.

Mrs. Thayer is now serving on the Camp Fire Board of Directors as Chairman of the Awards Committee. She is also Regional Representative from this district to the Regional Executive Committee of the National Council.

CONVENTION HIGHLIGHTS

The twenty-first annual meeting of the Woman's Auxiliary to the Arizona Medical Association has come and gone. To those members in attendance it was a most satisfactory, pleasant and stimulating convention. We were reminded that we, as well-informed Auxiliary members, can help further the aims of the medical pro-

fession and keep it from being enveloped by governmental restrictions.

The President, Mrs. Benjamin Herzberg and the State Convention chairman, Mrs. Joseph Kinkade, assisted by Pima County chairman, Mrs. Leo Kent, had the convention agenda well set up and it moved along smoothly and efficiently.

On Sunday Doctors and their wives began arriving at the Pioneer Hotel. Golf and swimming followed by a cocktail party at the Tucson Country Club was on the program, but due to the rain and cold weather only the cocktail party was held.

Mrs. Herzberg held her final Executive Board meeting on Monday night before convention opened. Dinner preceded the meeting at the Old Pueblo Club.

An eleven o'clock Brunch on Tuesday was the opening meeting of the Convention. This innovation was a success as it enabled more women to be on hand to hear the committee reports and the speaker of the day, Miss Lucia G. Allyn, State Supervisor of Nursing Education. Ninety-two women were in attendance.

On Tuesday afternoon, Mrs. Arthur A. Herold, our National President, arrived by plane from the Texas convention. That evening old acquaintances were renewed at one event that everyone attends, the Medical Association's cocktail party and dinner dance, at the Pioneer Hotel.

Wednesday morning we were honored by having Mrs. Herold as our guest at the 10 A.M. business session. The new officers had quite a thrill being installed by the National President. Seldom is Arizona honored by a visit from an officer living so far away, and we were proud to have Mrs. Herold hear the splendid reports of the County Presidents which showed so clearly the work which had been done during the year.

Following the session, everyone gathered at the El Rio Country Club, where at tables beautifully decorated in a May-Day motive, a delicious luncheon was served. Mrs. Herold was the guest speaker and inspired us all with a resume of the many opportunities which are presented to us as Doctor's wives to be of real service and influence in the problems and plans of the troubled world of today.

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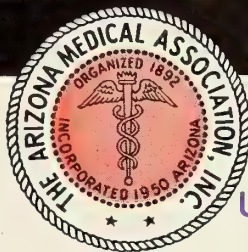
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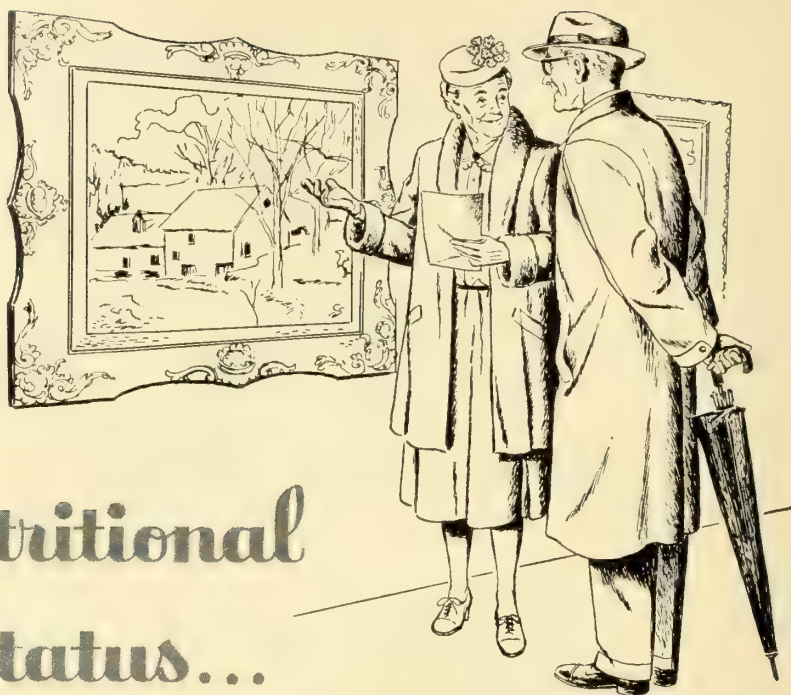
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INSURANCE

For Physicians, Surgeons, Dentists Exclusively

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\$5,000.00 accidental death	\$8.00
\$25.00 weekly indemnity, accident and sickness	Quarterly
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for protection of our members.
Disability need not be incurred in line of duty — benefits
from the beginning day of disability.

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49 years under the same management

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For **HIGH** Pollen Levels—

HIGH

Antihistaminic Potency

Neo-Antergan is characterized by high antihistaminic potency—and a high index of safety. It affords prompt, safe, symptomatic relief to the allergic patient during distressing periods of high pollen levels.

Neo-Antergan is *available on prescription only*, and is advertised exclusively to the medical profession.

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Available in coated tablets of 25 mg. and 50 mg. in bottles of 100, 500, and 1,000.

The Physician's Product

NEO-ANTERGAN[®]

MALEATE

(Brand of Pyrilamine Maleate)
(Formerly called Pyranisamine Maleate)

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IN HAY FEVER

Effective

even when the pollen count is high

TRIMETON, one of the more potent antihistamines, has consistently provided symptomatic relief in a high proportion of hay fever patients regardless of the pollen count.

In *severe* hay fever, at least 75 per cent of patients experience relief; as many as 90 per cent of patients with *mild* symptoms are benefited. A relatively low incidence of side effects assures uninterrupted therapy for optimum results.

TRIMETON[®]



(brand of propenpyridamine)

TRIMETON—indicated in all allergic states responding to antihistamines.

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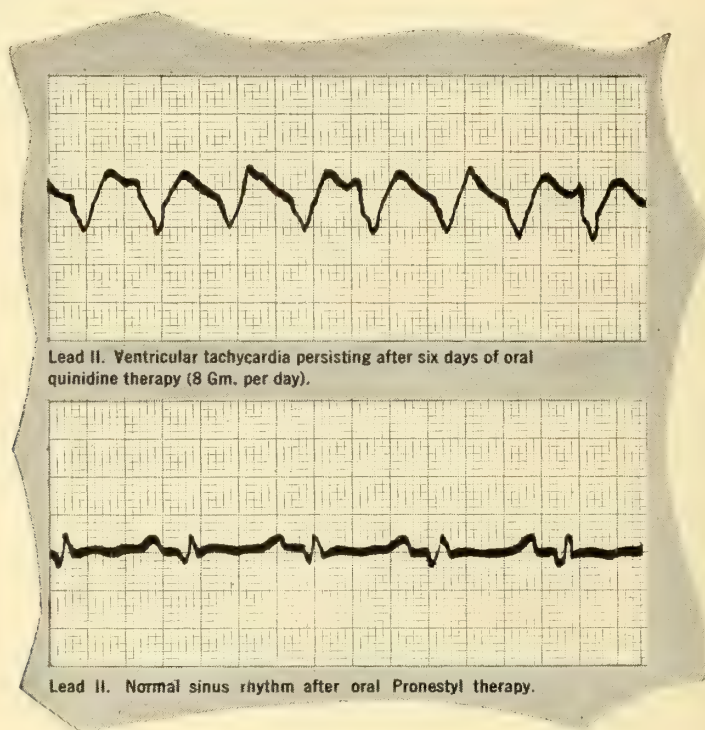


a **new** drug . . .

for the treatment of ventricular arrhythmias

PRONESTYL *Hydrochloride*

Squibb Procaine Amide Hydrochloride



Oral administration of Pronestyl in doses of 3-6 grams per day, for periods of time varying from 2 days to 3 months, produced no toxic effects as evidenced by studies of blood count, urine, liver function, blood pressure, and electrocardiogram. Pronestyl may be given intravenously with relative safety.

PRONESTYL IS A TRADEMARK OF E. R. SQUIBB & SONS

Pronestyl Hydrochloride Capsules, 0.25 Gm., bottles of 100 and 1000.
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For detailed information on dosage and administration, write for literature or ask your Squibb Professional Service Representative.

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BELIEVE IN YOURSELF!

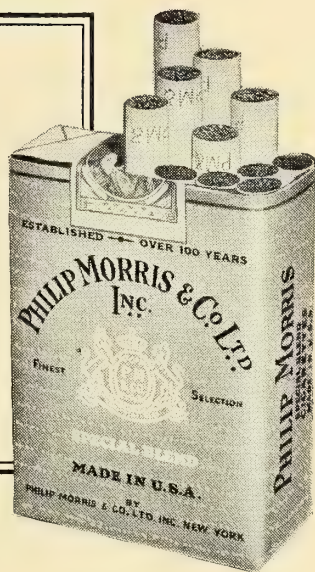
Doctor, you probably have read a great deal of cigarette advertising with all sorts of claims.

So we suggest: make this simple test...

Take a PHILIP MORRIS — and *any* other cigarette. Then,

1. Light up either one. Take a puff — don't inhale — and s-l-o-w-l-y let the smoke come through your nose.

2. Now do exactly the same thing with the other cigarette.



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**A
FACTUAL
REPORT
ON**

SUCARYL[®]

(CYCLAMATE, ABBOTT)

the new heat-stable, non-caloric sweetener

WHAT IT IS: SUCARYL is a new non-caloric sweetening agent useful in the preparation of sugar-restricted diets for diabetic and obese patients. Its function is to supply the desired sweetness without adding carbohydrate, thereby making it easier for patients to adhere to a strict dietary regimen. SUCARYL is heat-stable, which permits its use in boiling, baking, canning and freezing processes without loss of sweetness. As a result, SUCARYL can be used in a great variety of foods. It has a sugar-like sweetness and leaves no bitter or metallic aftertaste in ordinary use.

HOW SUPPLIED: Now in calcium as well as sodium forms. Handy-to-carry SUCARYL Sodium tablets, eighth-gram, effervescent, grooved, in bottles of 100 and 1000; SUCARYL Sodium Sweetening Solution, liquid form convenient for household use, in 4-fluidounce bottles; and SUCARYL Calcium Sweetening Solution, newly developed non-sodium form for low-salt diets, in 4-fluidounce bottles.

RECOMMENDED USAGE: Recommended daily limit for adults, 12 tablets or about 1½ teaspoonfuls of solution. Since the tablets contain sodium bicarbonate as a disintegrator, somewhat lower sodium diets are possible with the sodium solution than with the tablets. Sodium content per tablet is 21.64 mg., while an equivalent amount of sodium solution contains 14.25 mg.

Patients on strict low-salt diets, however, should use the calcium solution. The calcium form has a lower bitter taste threshold, noticeable in some foods when the proportion reaches 0.5 percent, compared to about 0.8 percent for the sodium form. Both forms are equally good in ordinary use.

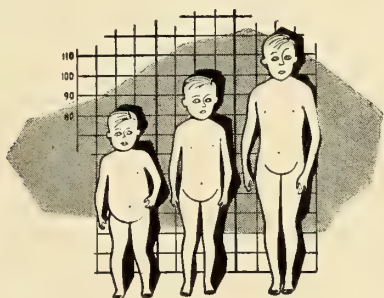
NEW, ENLARGED RECIPE BOOKLET is now available. Contains canning and freezing instructions, plus new recipes for cooked and baked foods sweetened with SUCARYL. Recipes save 15 percent or more in calories. To obtain copies for your patients, see your Abbott representative, or simply write "SUCARYL Recipe Booklets," specifying the number you need, on your prescription blank and mail to Abbott Laboratories, North Chicago, Illinois. Professional literature and a sample bottle of SUCARYL Sodium tablets also will be sent on request.

Abbott

AUREOMYCIN

Hydrochloride Crystalline

*Effective against many bacterial and rickettsial infections,
as well as certain protozoal and large viral diseases.*



The Pediatrician has found that aureomycin is promptly and fully effective in his young patients. Infections in any part of the respiratory tract, due to susceptible organisms, are as a rule readily controllable by its means, as are most meningeal infections caused by staphylococci, streptococci, pneumococci, *H. influenzae* and *E. coli*. In the infectious diarrhea of infancy, aureomycin, in conjunction with fluid and electrolyte replacement, has given excellent results. Aureomycin is a drug indispensable to pediatric practice.

Packages

Capsules: Bottles of 25 and 100, 50 mg. each capsule. Bottles of 16 and 100, 250 mg. each capsule.

Ophthalmic: Vials of 25 mg. with dropper; solution prepared by adding 5 cc. of distilled water.

LEDERLE LABORATORIES DIVISION

AMERICAN Cyanamid COMPANY

30 Rockefeller Plaza, New York 20, N. Y.

Meat . . . in the Low-Sodium Diet

Clinical experience^{1,2} and investigative data³ indicate that the liberal use of meat may not be contraindicated when sodium intake must be restricted. Because unsalted meat contains only relatively small amounts of sodium, while contributing importantly to other nutrient needs, meat deserves special consideration in very-low-sodium diets, in sodium-poor diets, and in no-extra-sodium diets.

Table I lists the amounts of sodium³ in three kinds of meat. Table II gives the estimated amounts of sodium in hospital diets planned for cardiorenal vascular patients.⁴

SODIUM IN MEAT³

	Sodium Provided by 60 Gm. Serving	Sodium Provided by 100 Gm.
Beef, without bone	32 mg.	53 mg.
Lamb, without fat	66 mg.	110 mg.
Pork, without fat	35 mg.	58 mg.

Table I

SODIUM IN HOSPITAL DIETS⁴

Sodium-Poor Diets*				Very-Low-Sodium Diet†
40 Gm. Protein	70 Gm. Protein	100 Gm. Protein	130 Gm. Protein	70 Gm. Protein
400 mg. Na	500 mg. Na	800 mg. Na	1,000 mg. Na	200 mg. Na

Table II

*Foods prepared and served without salt.

†Weighed diet. May contain 4 oz. of unsalted meat.

(Normal diets contain approximately 4 Gm. of sodium daily.)

Hence, the data here shown indicate that relatively generous amounts of meat may be included in low-sodium diets.

Meat serves well in the therapeutic objective of maintaining a high state of nutrition in patients with congestive heart failure or nephritic edema by providing valuable amounts of biologically complete protein and of B complex vitamins, including the recently discovered B₁₂.

1. Wheeler, E. O.; Bridges, W. C., and White, P. D.: Diet Low in Salt (Sodium) in Congestive Heart Failure, J.A.M.A. 133:16 (Jan. 4) 1947.

2. Wohl, M. G., and Schneeberg, N. G.: Dietotherapy (Cardiovascular Disease), in Jolliffe, N.; Tisdall, F. F., and Cannon, P. R.: Clinical Nutrition, New York, Paul B. Hoeber, Inc., 1950, chap. 27.

3. Bills, C. E.; McDonald, T. C.; Niedermeier, W., and Schwartz, M. C.: Survey of the Sodium and Potassium Content of Foods and Waters by the Flame Photometer, Fed. Proc. 6:402 (Mar.) 1947.

4. Mayo Clinic Diet Manual, Philadelphia, W. B. Saunders Company, 1949, p. 113.

The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.



American Meat Institute
Main Office, Chicago... Members Throughout the United States

A

*Preferred Nasal Decongestant
and Vasoconstrictor*

Otorhinolaryngologists frequently express preference for Neo-Synephrine hydrochloride to alleviate turgescence and nasal congestion in colds, sinusitis and various forms of rhinitis.

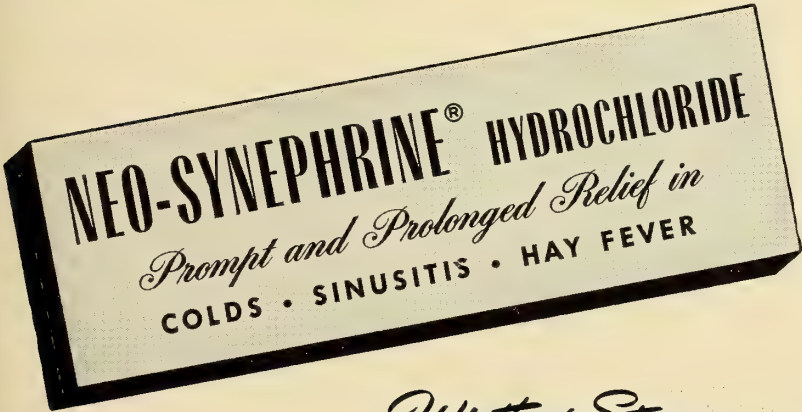
“When considerable nasal obstruction exists, relief may be obtained by the instillation of some shrinking agent into the nose . . . as for example Neo-Synephrine hydrochloride (¼ %)”¹

A “desirable preparation of this type has been perfected in Neo-Synephrine hydrochloride. It may be used for local application in the nose in ¼ to 1 % solution.”²

Neo-Synephrine’s “desired effect occurs within from two to fifteen minutes . . .”³

“Its action is sustained for two hours or more.”³

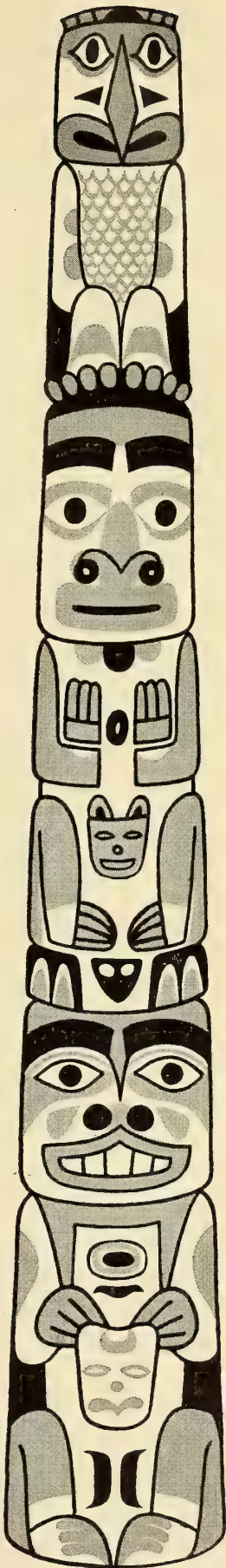
Neo-Synephrine hydrochloride is notable for freedom from sting and for effectiveness on repeated application. There are few complaints of after effects such as burning and nasal congestion . . . and little tendency to develop local sensitivity.¹



Winthrop-Stearns INC.
NEW YORK 18, N. Y. WINDSOR, ONT.

1. Tuft, L.: Clinical Allergy. Philadelphia, W. B. Saunders Co., 1947, pp. 335-336.
2. Hansel, F. K.: Allergy of the Nose and Paranasal Sinuses. St. Louis, C. V. Mosby Co., 1936, p. 769.
3. Kelley, S. F.: Choice of Sympathomimetic Amines, Cornell Conferences on Therapy, II, 1947, p. 156.

Neo-Synephrine, trademark reg. U. S. & Canada, brand of phenylephrine



ESSENTIALS OF AN ANTIBIOTIC

rapid absorption and distribution

in maternal body fluids and tissues

Rapid absorption and distribution following oral administration suggest the use of Terramycin as an effective aid in combating puerperal infection. Therapeutic serum and tissue levels are quickly achieved, to control many infectious processes which may complicate pregnancy or labor. In pyelitis of pregnancy caused by a sensitive organism, for example, patients respond to Terramycin "...very promptly..." with "...a prompt drop in temperature, disappearance of pyuria and bacilluria, and symptomatic relief."¹

CRYSTALLINE
Terra

broad antimicrobial spectrum

The antimicrobial spectrum of Terramycin encompasses pathogens responsible for many of the infections which may complicate pregnancy, e.g., streptococci, staphylococci, pneumococci, coliform bacteria, gonococci, and the viral-like causative agent in lymphogranuloma venereum.

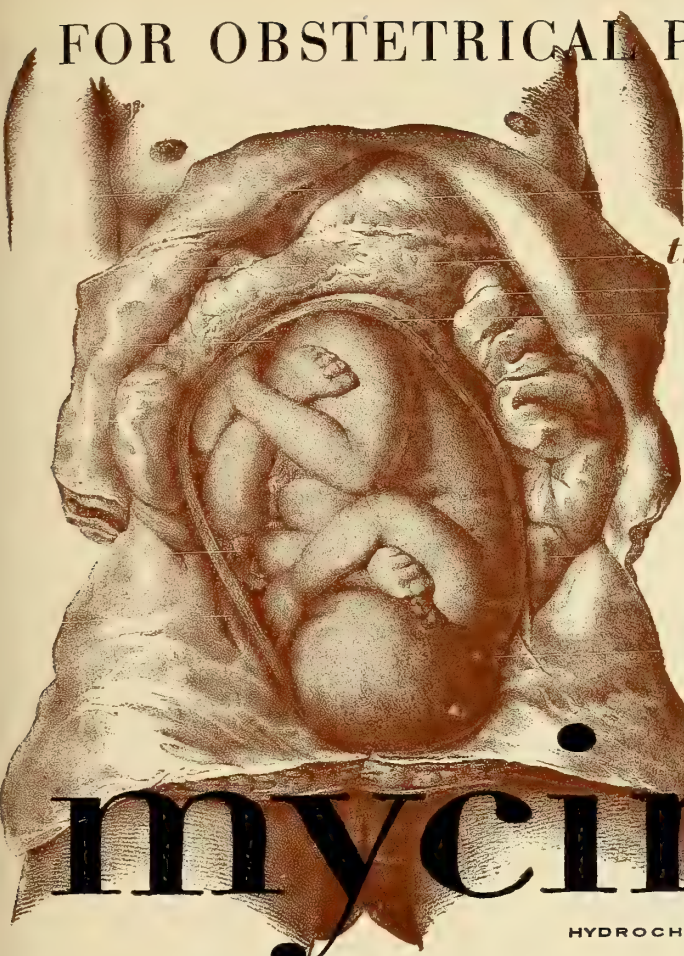
1. Douglas, R. G.; Ball, T. L., and Davis, I. F.:
California Med. 73:463 (Dec.) 1950.

2. Pratt, P. T.: Nebraska State M. J. 35:294 (Sept.) 1950.

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*rapid passage through
the placental membrane*

Terramycin readily traverses the placental membrane and becomes available in the fetal circulation to combat or prevent fetal infection, said to be a frequent cause of premature labor or abortion. In both mother and fetus "very prompt response" with Terramycin treatment has been recorded in pneumococcic pneumonia complicating pregnancy.²

mycin

HYDROCHLORIDE



The growing literature continues to stress:

1. The broad-spectrum activity of Terramycin

against organisms in the bacterial and rickettsial as well as several protozoan groups.

2. The promptness of response to Terramycin

in acute and chronic infections involving a wide range of organs, systems and tissues.

Crystalline Terramycin Hydrochloride is available as:

CAPSULES, 250 mg., bottles of 16 and 100; 100 mg., bottles of 25 and 100; 50 mg., bottles of 25 and 100.

ELIXIR (formerly Terrabon), 1.5 Gm. with 1 fl. oz. of diluent.

INTRAVENOUS, 10 cc. vial, 250 mg.; 20 cc. vial, 500 mg.

CHAS. PFIZER & CO., INC., Brooklyn 6, N.Y.

MILD HYPERTROPHIC ARTHRITIS OF LUMBOSACRAL JOINT and TENDERNESS OF ERECTOR SPINAE MUSCLES

Photograph of patient 27 years old. Trouble began nine months ago when lifting her baby as it grew toward one year of age. Back pain at lumbosacral joint is persistent; radiating to the abdomen. Made worse by cold damp weather and prolonged walking.



Patient experiences great relief with application of Camp reinforced Lumbo-sacral Support. Rest and support is given to the lumbosacral joint, its ligaments and to the erector spinae muscles, thus improving the body mechanics, note especially the decreased dorsal curve. The downward pull of the gluteal muscles on the posterior crests of the ilia is relieved.

**Camp Orthopedic Supports help many patients
suffering from osteo-arthritis of the spine**

When the dorsal region of the spine is involved, higher supports than the one illustrated are provided by Camp.

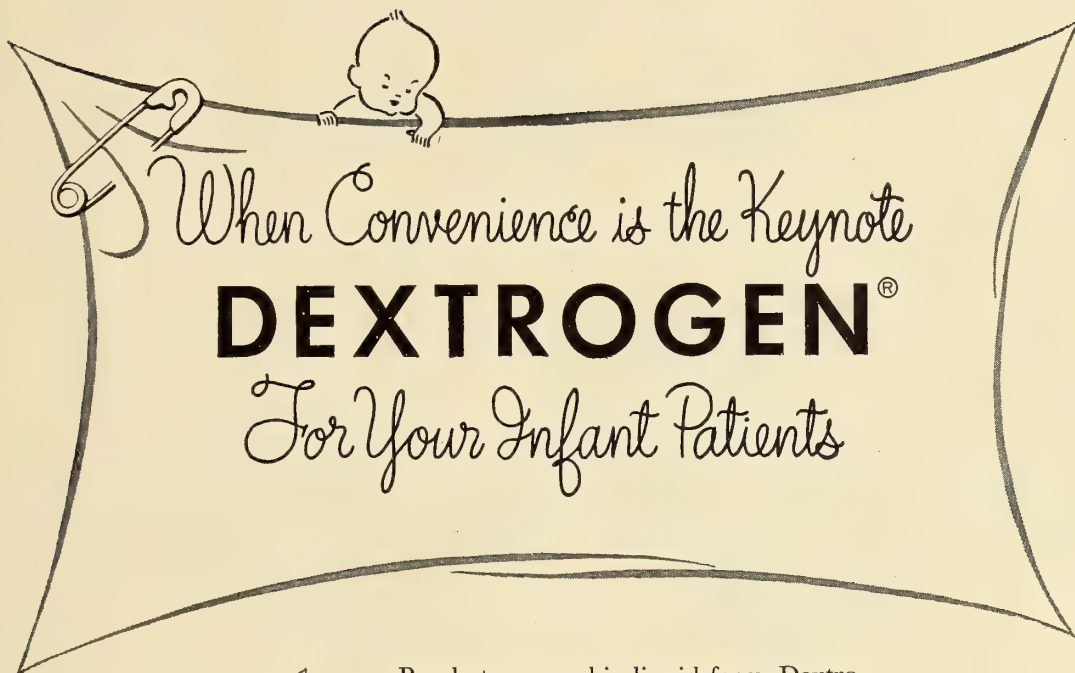
All lend themselves readily to reinforcement.

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The higher protein content of normally diluted Dextrogen—2.2% instead of 1.5% as found in mother's milk—satisfies every known protein need of the rapidly growing infant. Its lower fat content makes for better tolerability and improved digestibility.

Dextrogen serves well whenever artificial feeding is indicated, and is particularly valuable when convenience in formula preparation is desirable.

*Applicable third week and thereafter; 1:3 for first week, 1:2 for second week.

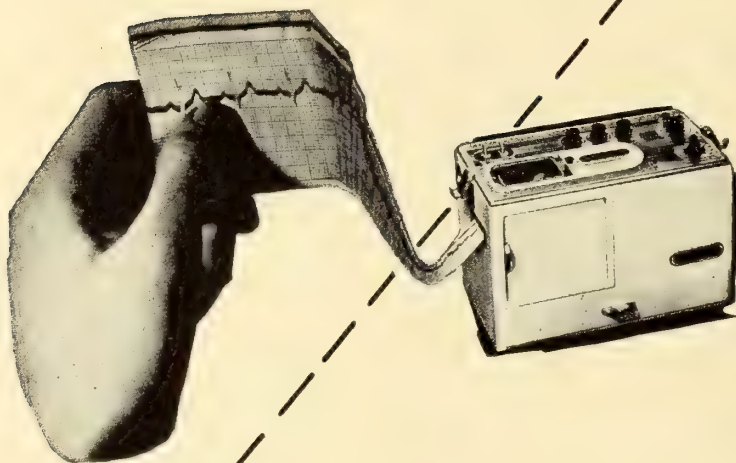
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All the mother need do is pour the contents of the Dextrogen can into a properly cleaned quart milk bottle, and fill with previously boiled water. Makes 32 oz. of formula, ready to feed.*

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Harding, F. E.: West. J. Surg. Obst. & Gynec. 52:31 (Jan.) 1944

"All patients (53) described a sense of well-being" following "Premarin" therapy for menopausal symptoms.

Neustaedter, T.: Am. J. Obst. & Gynec. 46:530 (Oct.) 1943.

"It ('Premarin') gives to the patient a feeling of well-being"

Glass, S. J., and Rosenblum, G.: J. Clin. Endocrinol. 3:95 (Feb.) 1943

"General tonic effects were noteworthy and the greatest percentage of patients who expressed clear-cut preferences for any drug designated 'Premarin.'"

Perloff, W. H.: Am. J. Obst. & Gynec. 58:684 (Oct.) 1949.



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1. Nettleship, A.: Arch. Dermat. & Syph. 61:669, 1950
2. Brewer, W. C.: Arch. Dermat. & Syph. 61:681, 1950

Sopronol therapy is a therapy of choice with physician after physician.

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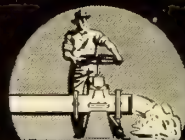
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From The Literature

- Bubert and Cook, Bulletin of School of Medicine, Univ of Maryland, Vol. 32, pp. 175-190, 1948.
- Paul and Montgomery, J. Iowa State Med. Soc., June, 1948.
- Krantz, Holbert, Iwamoto and Carr, J.A.Ph.A., Vol. 36, pp. 248-250, 1947.
- New and Non-official Remedies, 1950, p. 285.



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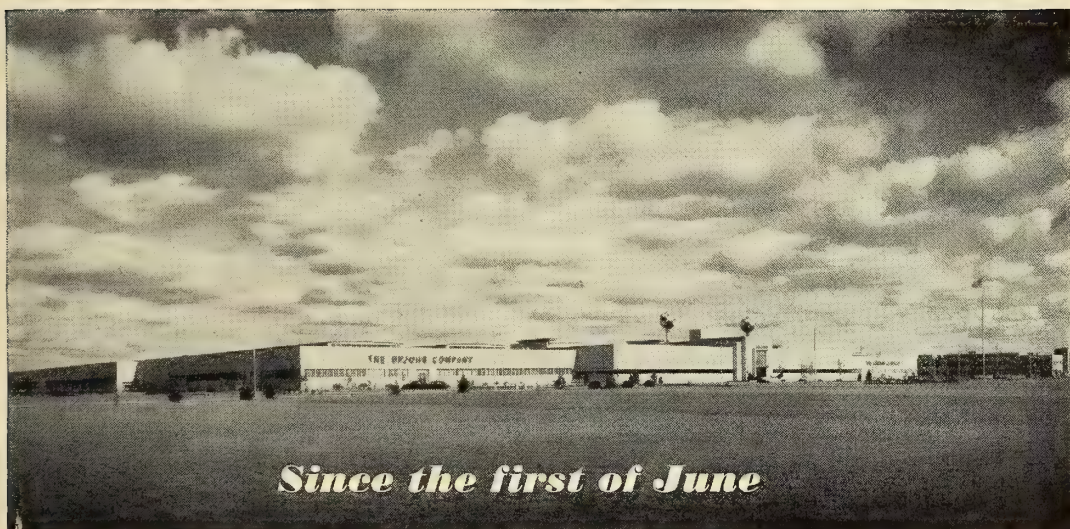
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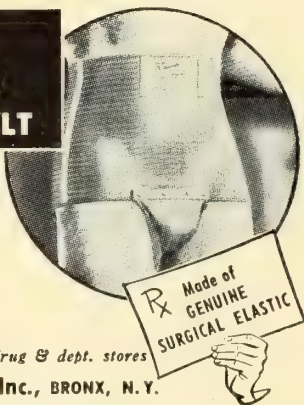
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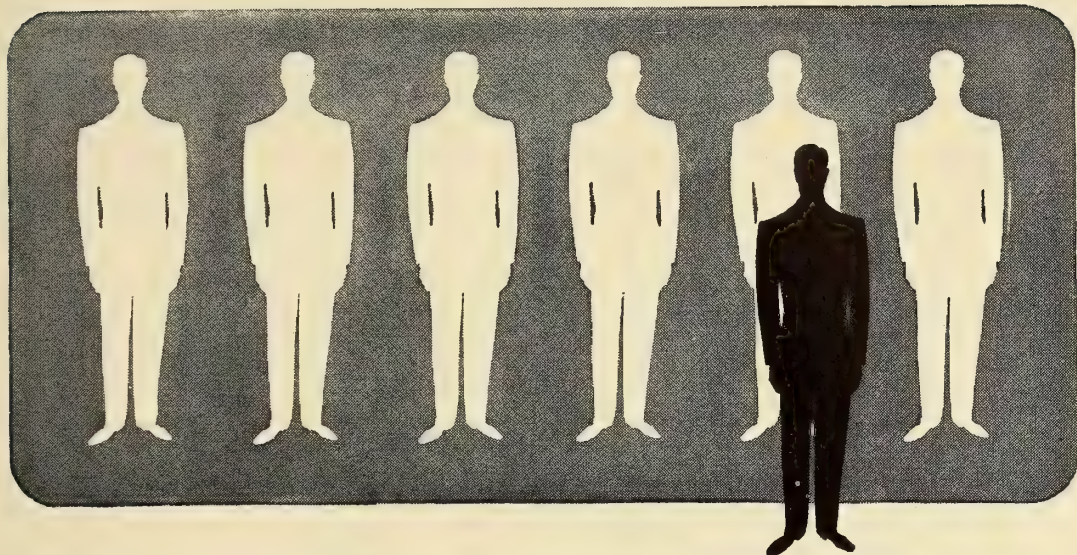
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TULAREMIA WITH REPORT OF SIX CASES

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It is not the intension in this report to make a review of the problem of Tularemia but to call attention to the disease as it is found in Arizona, and to report six cases seen since 1947.

Since 1940, there have been but thirteen cases reported to the Arizona State Department of Health. (1) However, there must have been more cases than thirteen observed during that time because seven cases have been seen in Mesa since 1947, six of which are being reported in some detail in this paper. I know of three other cases which have been treated in Tempe, Arizona during this same period.

This disease is caused by a small pleomorphic non-motile, gram-negative bacterium. The organism was first definitely described and identified by McCoy and Chapin (2) in 1911 in Tulare County, California, as obtained from dead ground squirrels.

The first reported death from this disease was by Francis (3) in 1920 when he was investigating rabbit fever in Utah. He discovered that the blood of a rancher, who had been bitten on the neck by a deer fly, when injected into a guinea pig produced the plague-like disease described by McCoy. Francis reports that there are at least twenty methods known by which man may be infected with tularemia. The most common methods, we believe, are from the cotton-tail rabbit, jack rabbit, snowshoe hare, bites of ticks; namely, wood tick and dog tick, fleas, and deer flies. Also by bites from such animals as cats, opossums, dogs, coyotes, squirrels, hogs, sheep, and goats. He states that no human infections have been traced to the domestic rabbits; however, one of our cases gave a history of skinning a tame rabbit about ten days before the onset of his illness.

It is suggested this is truly an American disease because the organism was first described here and the first reported death was in the United States. But tularemia as an endemic disease of man has been observed in forty-six states and in Alaska. It has been reported from Canada, Japan, Soviet Union, and in recent years, in epidemic proportions from Europe. Dr. Rosen, a physician who, as a boy, lived in Tulare County, California where he has since practiced many years (2) states he has seen only one case of tularemia in that county and that is the only case reported in Tulare county since 1940 except one other questioned report. So he concludes it must be rare in the place of its scientific birth.

In contrast to the few cases seen in Tulare, California, it is of interest to note the frequency with which it is reported in Arkansas (4). In the ten year period from 1938 to 1948 there were 1,231 reported cases. A point of interest is that in that state the disease is definitely an occupational hazard and the Arkansas State Board of Health reports the chief source of the infection was tick bite. Only twenty percent of their cases were infected by direct contact with rabbits. This is in contradistinction to the more common opinion that ninety percent of the disease is rabbit borne.

These authors emphasize the fact that tularemia constitutes an occupational hazard to certain groups of laborers. They further state tularemia is nowhere classified as an occupation disease; however, two of the cases which will be reviewed here were accepted by the Arizona Industrial Commission as occupational hazards and were so handled.

There is some difference of opinion as to the dependability of laboratory procedures used in

Read before the Annual Meeting Arizona Medical Association, Phoenix, May 3, 1950.

arriving at a diagnosis of tularema. Some investigators (6) believe, the diagnosis is best made by a blood serum agglutination test using *B. tularensis* antigen. The agglutinins are generally absent from the blood during the first week of the disease appearing in increasing concentration from the second week on to reach a maximum concentration in from four to seven weeks (7, 8). Agglutinins for the *Brucella* organisms may develop in tularemia. If the infection is primarily caused by *Pasteurella tularensis*, a higher titer for that organism should be present. It is reported that cross agglutination with the *Brucella* occurred only in sera which agglutinated tularensis in dilution of 1:320 or over. It is suggested for a diagnosis, a titer of at least 1:80 should be present. A marked rise in titer, especially when the patient is improving clinically, is the more diagnostic of all the laboratory methods except by animal inoculation of sputum, blood, or material aspirated from a lymph node or the lung.

There are several forms of the disease described but the majority of the cases can be divided into: 1—ulceroglandular; 2—the typhoidal type (four cases being presented here of this type), and 3—pneumonic type (two cases being presented are of this type.)

There were 268 reported cases of tularemic pneumonia up to 1945 (10) and of these cases, 161 recovered, resulting in a mortality rate of forty percent. This, of course, was before streptomycin was available. Hunt (11) of Vanderbilt University, reporting in 1947, had treated twelve cases of pleuropulmonary tularemia with streptomycin in doses 0.4–1.6 grms, daily for three to nine days. He concluded the rapid disappearance of tularensis from the sputum or pleural fluid as determined by animal inoculation, indicated that the organism was rapidly killed in the tissues.

CASE NO. 1

This is a case of a twenty-three year old Mexican laborer who entered the hospital on April 13, 1947 complaining of severe headache, high fever followed by chills, heavy perspiration, and generalized body aching. There was also a history of slight injury to the chest which somewhat confused the picture.

Physical examination at the time of admission revealed a patient who appeared to be extremely uncomfortable and in pain. There were no significant physical findings. There were no

open lesions, no palpable glands and the spleen was not palpable. The leukocyte count was 9,000 per cubic millimeter. The differential blood count, the erythrocyte count, and the mazzini test were normal. The urine was normal. On the following day agglutination tests were normal for typhoid, paratyphoid and OX-19. The *Brucella abortus* agglutination reaction was positive in 1:1280 dilution. It was, therefore, concluded that this patient had Malta fever for which he was treated with penicillin and sulfadiazine. He was given 6.8 grams of streptomycin before the diagnosis of tularemia was established. It was given along with penicillin and sulphanilimide. The diagnosis of Malta fever was kept for ten days. During this time the patient continued to have severe pain, generalized aching, severe headaches (retro-orbital in location), and profuse sweats followed by chills, and, at times he was not entirely national. We then felt that there was another element to this case which had been missed. The agglutination tests were repeated, this time including tularemia. The patient had been closely questioned and he rigorously denied dealing with wild or tame animals in any way until he was reminded by a friend that he had skinned a wild rabbit. He then remembered the incident and recalled getting blood on his hands from the rabbit. The agglutination test for tularemia was positive in 1:2560 dilution. At this time the leukocyte count was 23,000 per cubic millimeter with seventy-six per cent polymorphonuclear cells. The hemoglobin was seventy-three per cent. A blood culture reported May 11, 1947 stated, "Culture shows somewhat non-motile, gram negative bacillus morphologically similar and culturally characteristic of bacteria tularensis." A blood culture taken ten days earlier was also reported as containing bacteria tularensis.

By this time the patient had become more ill and required more sedation. He had marked perspiration, lost ten pounds, developed palpable axillary glands, bilateral inguinal glands, and his spleen was palpable. Roentgenogram of the chest reported on April 26, 1947, "No abnormalities."

After receiving the report of the positive agglutination test for tularemia streptomycin was given (.2 grams q4h). The penicillin and the sulfanilamide were discontinued. During the first ten days of the streptomycin therapy the

patient's temperature ranged from 100 to 103 degrees Fahrenheit. On May 9 the temperature was normal and it remained so during the remainder of his stay in the hospital. Within two or three days after streptomycin therapy the patient began to feel better; the perspiration stopped, the chills subsided (chills that had been so severe as to shake the bed), and his appetite improved. He required less sedation and codeine for the control of pain. A repeat agglutination reaction for tularemia was reported on May 10, 1947 as positive in 1:6000 dilution and the *Brucella abortus* reaction was positive in 1:40 dilution. We believe that this was, without question, a case of tularemia. The patient had a satisfactory response to the use of streptomycin. He fulfilled the criteria required by some investigators of this disease as he improved clinically. There was a very definite increase in the serum agglutination titer which was quite pronounced and rapid. It is suggested by Dr. D. T. Smith of Duke University that such a rise may result from the antigenic stimulus provided by destruction of large numbers of organisms in rather a short period of time such as is probably accomplished with streptomycin. This patient had a total of 19.2 grams of streptomycin. The administration of the streptomycin definitely produced the turning point in this case, and it is not unlikely that the patient might have expired without its use.

CASE NO. 2

This is a case of a forty-two year old farmer who was seen in the office March 30, 1948, at which time he was complaining of severe body aching, headache, weakness, heavy perspiration, and chills. At the time of admission to the hospital there were no significant physical findings except that he was extremely ill and unquestionably in a state of dehydration. The temperature was 101 degrees Fahrenheit. The erythrocyte count was 4,200,000 and the leukocyte count was 9,400. The hemoglobin was 94 per cent. There were 33 per cent lymphocytes and 66 per cent polymorphonuclear per cubic millimeter. The urine was normal except for an occasional white blood cell, and the mazzini test was normal. This patient was specifically asked if he had been hunting, shooting squirrels or rabbits, or had in any other way come in contact with wild animals. This he explicitly denied. The agglutination tests for typhoid, paratyphoid, OX-19, *Brucella abortus*,

and the routine leukocyte count, erythrocyte count, and sedimentation rate were ordered; all including *Brucella abortus* were negative. The agglutination test for Tularemia was not given. He was given penicillin, but failed to show any improvement. He continued to have most severe pain, retro-orbital headaches, and severe chills with heavy perspiration to the extent that frequent change of bed linen was required. His temperature fluctuated between 99 and 103 degrees Fahrenheit. He was disoriented and did not know that he was in the hospital. He did not recognize his brother who spent considerable time at his bed side.

After a week of penicillin therapy and the failure of any abatement of symptoms or progress in the case and in spite of his denial of having had contact with any wild animals and his statement that he had not been away from his ranch or the town of Gilbert, agglutination tests for paratyphoid, typhoid, *Brucella abortus*, OX-19, and Tularemia were ordered April 7. The agglutination reaction for Tularemia was positive in a titre of 1:640. There was a negative *Brucella abortus* reaction. On April 8 streptomycin was begun (.2 grams, q4h). The temperature began to level off and at the same time the patient began to feel better. He cleared mentally, his fever and chills subsided and there was definite improvement. When he was feeling well again and mentally clear, he was again asked about the handling of any rodents or rabbits, and at this time, he remembered having skinned some tame rabbits for a neighbor about two weeks prior to the onset of his illness. April 12 the Tularemia agglutination titer was 1:320. The increase in the serum agglutination titer as was seen in our previous case was not present. At no time was there an external lesion. There were no palpable lymph nodes and the spleen was not palpable. The most characteristic factors of this patient's illness was the extreme headache, retro-orbital in location, marked muscle soreness, and heavy perspiration, chills and fever. One year later the agglutination reaction for Tularemia was positive in 1:320 dilution. It was several months before he gained back his strength and vitality. The patient received a total of 8.4 grams streptomycin.

Note: As was mentioned earlier in this paper Francis states: "No human infections have been traced to domestic rabbits," however, it is most

difficult to deny that Tularemia was contacted from the neighbor's rabbits in this case.

CASE NO. 3

This is a case of a fifty-eight year old male farmer from Tempe, Arizona. He came to the office November 22, 1948 complaining of severe body aches and pains, headache, weakness, chills and fever. This man reminded us so much of the case just presented that the first question we asked him was, "Have you been out hunting?" He admitted that about one month previously he had been hunting and had killed and skinned a deer. About ten days previous he had killed and skinned an elk. This man was sent directly to the hospital. Agglutination tests for typhoid, paratyphoid, OX-19, Brucella abortus and Tularemia were requested and all the reactions were negative except the Tularemia reaction which was positive in 1:640 dilution. The erythrocyte count was 3,920,000 and the leukocyte count was 7,350 per cu. mm. The mazzini test was negative, and the urine was normal except for occasional white blood cells per high powered field. The patient was promptly given streptomycin (the usual dosage of .2 grams q4h). The temperature came down to normal the first day after the streptomycin was begun. It went back to 102 degrees Fahrenheit the first afternoon, then gradually came to normal and remained so throughout his stay in the hospital.

This man also had very severe headaches and generalized body pain with the usual chills and fever. A roentgenogram of the chest, taken November 23, 1948, was reported as "healthy chest". This patient had a total of 9.6 grms. of streptomycin. He left the hospital feeling well.

Another case, observed by others, was in the hunting party with the above patient. This person ate some elk meat not long after which he, too, contracted Tuleremia. He was successfully treated with streptomycin.

CASE NO. 4

This is a case of a forty-five year old sheep inspector for the state of Arizona. This man first presented himself at the office complaining of generalized aches and pains, a feeling of fatigue, and of simply being "sick" all over. He had fever and chills so severe that they shook his bed while he was at home. At this time he started to complain of a non-productive cough and pain in the chest. When examined in the office he had a dusky, cyanotic appear-

ance. He was extremely uncomfortable and complained of painful respiration. Examination of the chest revealed moderate splinting of the chest with some limitation of excursion of the left diaphragm. There were many fine crackling rales at the left base. He had an almost continuous, hacking dry cough. He was hospitalized with a temperature, at the time of admission, of 100 degrees Fahrenheit. The erythrocyte count was 3,950,000 per cubic millimeter and the leukocyte count was 10,000 per cubic millimeter. The mazzini test was negative. The specific gravity of the urine was 1.003 and it contained an occasional leukocyte per high powered field. The agglutination reaction for Tularemia was positive in 1:640 dilution. The agglutination reactions for typhoid, paratyphoid, Brucella abortus and OX-19 were normal. A roentgenogram of the chest was reported March 8 as—"AP and lateral chest films show infiltrative shadows of increased density involving most of the left lower lobe. The left diaphragm is flattened, the costophrenic sinus partially obliterated by pleural thickening which the lateral view shows to be situated anteriorly. The right lung field, the ribs and the heart are normal. IMPRESSION: Pneumonia, either atypical or viral or a bronchopneumonia."

Streptomycin therapy was started (.2 grams q4h). The temperature started to decline and did not again go above 100 degrees Fahrenheit and on the fifth day of streptomycin therapy his temperature reached normal and remained so throughout his stay in the hospital. The patient's most distressing symptom was painful respiration made worse by coughing. He had begun to have a moderate amount of mucopurulent sputum. He had such a degree of pain in his chest that he required a considerable amount of codeine for relief of pain and he moved very little about in the bed because of his pain.

Additional roentgenograms were made of his chest which showed a rather slow improvement; however, there was definite evidence of clearing. On March 11, the films revealed that the pleural reaction at the left costophrenic sinus had not changed and that there was no free fluid present.

This patient had been inspecting a flock of sheep and goats down in the Wilcox area about ten days before the onset of his symptoms. This patient left the hospital on the 17th of March free from any pain, his cough had

not entirely subsided, and he still complained of marked weakness. For several weeks he was too tired and weak to attend to his duties as a sheep inspector. After several weeks a roentgenogram revealed the lung fields to have entirely cleared. This patient had a total of 13.2 grms. of streptomycin. This is one of the cases which was accepted by the State Industrial Commission as a compensable case.

This case is very suggestive as Reimann (9) states that the pathogenesis of primary pulmonic tularemia is apparently inhalational in mode, such as inhaling bacilli suspended in the air as dust, in droplets from patients or animals who have Tularemic pneumonia, or from handling dried cultures of the organism.

CASE NO. 5

This is a case of a thirty-two year old nurse's aide who presented herself in the office complaining of sore, fatigued muscles and joints. She stated she had not been well for the past three or four weeks. She was a nurse's aide at the hospital. This patient had, about fourteen months previous to this time, a breast amputation for adenocarcinoma of the left breast. On May 3rd she complained of very severe headaches during which she stated she could not think clearly. She complained of very severe generalized aching with fever followed by chills and a feeling of "heaviness" in the chest. The physical examination at the time she was seen in the office revealed some rales in the left lower base. She had marked tenderness on motion of joints and muscles and complained of "hurting" even when changing position. There were no other significant physical findings, no palpable mass in the abdomen, no palpable glands and the spleen was not palpable. There were no skin lesions or nodules. This patient was hospitalized. Roentgenograms of the chest failed to reveal a shadow of the left breast. There had been no appreciable change in the appearance of the lung field since the film made on April 2, 1948.

At the time of admission the erythrocyte count was 3,890,000 per cubic millimeter and the leukocyte count was 5000 per cubic millimeter. The differential count was normal and the mazzini test was negative. The urine contained a few white blood cells per high powered field. Blood agglutination reactions at that time were negative for typhoid, paratyphoid, *Brucella abortus* and the proteus OX-19 reaction was of 1:80.

A Tularemia agglutination reported the following day, May 6, was positive in a 1:320 dilution. Roentgenographic examinations two days after her admission were reported as, "Re-examination of chest shows infiltrative area of almost homogeneous density which involves the lower half of the left upper lobe and on AP film extends some just above the diaphragms to reveal the seventh rib posteriorly. The costophrenic angle is clear. There is, also, some increase in the hilar shadow on this side. The right lung field is clear." He also states that "A review of a film made May 3, 1949 shows that at that time there were several ill-defined, streaky shadows of increased density in the left lower lung field, which were overlooked at that time. These probably represent the beginning of the present process".

On May 11 there was a repeat agglutination reaction which was positive in 1:320 dilution for Tularemia which was also positive in the same titer of May 16. The sputum examination on May 11 revealed mixed bacteria. Blood culture report of May 31 was negative. This blood culture was reported on May 31, but taken during her stay in the hospital. This patient was started on streptomycin therapy May 5, the usual dosage of .2 grams q4h. The temperature was of a septic type of fever from the time of her admission until the fourth day of the streptomycin therapy. On the sixth day of treatment the temperature came to normal and remained so throughout her stay in the hospital. This patient, as did our previous patients, complained of severe muscular pains and headaches and during the first four or five days in the hospital, she continued to have severe chills with heavy perspiration and a dry non-productive cough. There was definite dulling of her sensorium. By the fifth day in the hospital on streptomycin therapy her symptoms had begun to subside, there was much less muscle and joint soreness. She began to eat better, her cough had begun to improve, and by this time she had developed some palpable nodes in the axillary and cervical regions. At no time did she have a palpable spleen. There was never a body rash or any kind of skin lesion. This patient presented somewhat of a problem to us because she emphatically denied having had contact with any kind of domestic animals or wild animals for the past several months. No animals had been brought into the home. We

began to speculate as to how she contacted this disease. We felt the diagnosis was dependable. She had a positive agglutination with increase in titer as she progressed and recovered from the disease. She had the typical set of symptoms that our previous patients had. She presented roentgenographic findings similar to the case last reviewed and as we stated, she was a nurses' aide and had given a lot of care to the patient who had recovered a month before from pulmonary Tularemia. The date of onset of symptoms was indefinite; however, she gave the onset of her feeling sick and achey and her muscular pains about three to four weeks after she had last attended the case which was just previously reviewed. We could see no other explanation than that this patient probably contracted Tularemia from this first case of pleuropulmonary Tularemia. We came to this conclusion after a lot of thought and consideration, and realizing there has been no reported case of proved human case-to-case transmission. However, it is suggested because of increasing pulmonary Tularemia, transmission by way of the patient's sputum is not impossible. (3) There was recently reported by Aagaard (5) the case of a graduate student in bacteriology who contracted Tularemic pneumonia after a rabbit sneezed in his face. This case just presented was reported to the Industrial Commission and was accepted and cared for on the same basis as the previously reported one.

This patient had a total of 8.4 grams of streptomycin. She was away from her job for several weeks after discharge from the hospital with complaints of weakness and muscle soreness. She is back on her job as a nurses' aide in our local hospital and is observed from time to time with a good bit of interest from the standpoint of her Tularemia as well as the adenocarcinoma of the breast.

CASE NO. 7

This is a case of a twenty-six year old veterinarian from Safford, Arizona who was seen in Mesa, January 5th in a private home. The patient had come to Mesa to attend the Arizona State Veterinary Convention. He states he was essentially well until December 31, 1949 when he began having generalized body aching, headaches of increasing severity, retro-orbital in location. He had fever, profuse perspiration and chills.

One interesting side light on this patient's his-

tory is that about three weeks before the onset of his present symptoms he had been vaccinating cattle for Bangs disease and had used a designated "Strain 19" brucella abortus vaccine, which is an attenuated strain, and some squirted into his eye accidentally. Because of this history, his local doctor did agglutination tests for *Brucella abortus*, the reports for which were not available at the time he left his home to attend the state convention in Mesa. However, a day or two after the onset of symptoms they subsided and the patient felt well enough to leave home and come to the convention.

On the basis of the possibility of his having contracted *Brucella abortus* from the manner in which he was accidentally vaccinated, and because of the severity of his symptoms, it was decided to treat this man with chloromycetin. After two days treatment in the home, the patient became worse. His pain became almost unbearable and the headaches were severe. He had severe chills, fever and perspiration. He was extremely uncomfortable and at times not entirely rational. He was hospitalized January 7, 1950.

Agglutination reaction for Tularemia, reported on January 8, 1950, was positive in a dilution of 1:320. The report was made available about noon on the eighth at which time streptomycin therapy (.2 grams q4h) was begun. The temperature on the morning of the 9th had reached normal and remained essentially normal during his stay in the hospital. The erythrocyte count was 4,600,000 and the leukocyte count was 7000 per cubic millimeter. The reaction for *Brucella abortus* was negative and it was later found that the blood sent to the Arizona State Laboratory by his local doctor was also negative for *Brucella Abortus*. On January 11, 1950 an agglutination titer of 1:160 for Tularemia was reported.

This man left the hospital on January 13, 1950 after five days of essentially normal temperature. He received a total of 7.2 grams of streptomycin. He returned to his home in Safford and two or three weeks time elapsed before he felt strong enough to return to his regular work.

CASE NO. 7

The seventh case in our series is not being reported in detail because part of the pertinent laboratory data was lost from the record.

SUMMARY

1. A brief review of tularemia has been pre-

sented—with the report of six additional cases. All six cases successfully and promptly responded to treatment with streptomycin.

2. Tularemia may be more common in the state of Arizona than is indicated by the number of cases which have been reported to the State Health Department since 1940. One case presented was probably contracted from a tame rabbit.

3. Two cases of pleuropulmonary tularemia have been presented, one of which seems to be from direct contact with another known case of tularemia—a situation not known to have been

previously reported. This case seems to favor an inhalation method of infection.

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RHEUMATOID SPONDYLITIS

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Rheumatoid spondylitis is a chronic, progressive, crippling disease involving the spinal column and its adjacent structures. Numerous synonyms can be found in the literature; however, some rheumatologists endeavor to make a distinction between certain ones, but there are no definite clinical differential points. The lack of uniform terminology has produced the following synonyms: spondylitis ankylopoetica, spondylarthrititis, Von Bechterew's disease, Marie-Strumpell's disease, ankylosing spondylitis, rhizomelic spondylitis and atrophic spondylitis.

The initial description of this disease was published by Von Bechterew in 1893, at which time he also emphasized its neurological manifestations. The next clinical reports of the characteristics of this disease were given by Strumpell in 1897 and Marie in 1898. Since then much has been compiled in the literature, especially during the past decade. None of these have given the answer to its etiology or specific treatment.

ETIOLOGY

Many rheumatologists feel that the onset of rheumatoid spondylitis is usually preceded by an acute or chronic infection or by recurrent bouts of acute infections with arthritic manifestations. On the other hand, preceding acute or chronic trauma to the spine may be the outstanding possible etiological factor, but as shown by Boland and Present (1), it is not always possible to incriminate a precipitating factor, as in one series he found 80% did not

give possible immediate cause and the remaining 20% gave no constant cause.

Many patients feel that their spondylitis is due to an injury, even though at the time of their injury roentgenograms of the spine revealed moderate or advanced changes consistent with long standing rheumatoid spondylitis. It is difficult for the physician as well as the patient to understand how a process of this nature may be present for months or even years before symptoms become evident. However, it is true that many cases of spondylitis are brought to light by insignificant trauma. Is it not logical for an individual with the susceptible spine to develop spondylitis, whatever the inciting cause, be it infection, exposure, psychic strain, or trauma?

PATHOLOGY

The important lesions involving the spine in rheumatoid spondylitis are inflammatory and progressive in nature, attacking the synovial joints; usually beginning in the sacro-iliac joints and then progressing upward to involve the diarthrodial or apophyseal joints of the lumbar, thoracic, and cervical spine, and the paravertebral ligaments and muscles; later involving the costovertebral and costochondral articulations. However, this process may begin in any region of the spine, nor does it necessarily follow this sequence of progression. In the early stages the diarthrodial joints present a synovitis with roughening of their articular cartilage, destruction of the cartilage, fibrous ankylosis, and eventually, bony ankylosis. One commonly sees spasm and contractions of the paravertebral

muscles. Calcification of the paravertebral ligaments frequently occurs, giving the characteristic "bamboo spine." This may produce kyphosis, or the stiff, straight "poker spine". The intervertebral disks are not affected in this process; however, it is common to have mild or marked decalcification of the vertebral bodies.

CLINICAL MANIFESTATIONS

Age. The usual age at onset of symptoms in rheumatoid spondylitis is during the third to fourth decade, the largest majority falling in the third decade of life; however, the initial symptoms may begin at any age. There is no particular age difference at time of onset in male or female.

Sex—The approximate ratio between male and female is nine to one. The significance of this is not clear. If trauma is considered as an etiological factor this may partially explain the difference because of more arduous activity on the part of the male.

Incidence—Incidence of rheumatoid spondylitis to rheumatoid arthritis of peripheral joints has been reported as 1:6⁶, 1:11², 1:13⁹, 1:19⁵. A higher ratio was observed in the armed forces, approximately 1:3¹. Rheumatoid arthritis of the peripheral joints is present in about 20% of the cases of rheumatoid spondylitis.

Onset—in approximately 90% of the cases of rheumatoid spondylitis the onset is insidious and progresses slowly, with frequent remissions and exacerbations. The beginning is usually in one or both sacro-iliac regions, producing muscular spasm, soreness, and tenderness in this area which is associated with slight to marked stiffness in the same area. In a small minority of the cases the onset is acute, and rapidly progressive.

Symptoms, signs, and course—Episodes of low backache and stiffness are the dominant complaints, and these frequently last from a few to several days and then subside. These attacks are frequently called lumbago, and they become more frequent and more intense. At first these tend to be relieved by aspirin and local heat, while at other times relief is obtained by mild exercise or rest. These symptoms are usually more pronounced in the morning on arising, with physical inactivity and damp weather. The pain and stiffness later become more persistent and are frequently associated with catches or sharp pains in the low back region, and the usual measures bring relief less

adequately. The patient finds it very difficult to describe his pain except that it is a tired, sore, deep ache with variable tenderness and stiffness across the low back and is aggravated or brought on by sudden physical exertion, lifting, bending, twisting, jolting, and sneezing or coughing. Occasionally on retiring at night the patient feels well, to be awakened in the early morning hours with low back pain. Sciatic pain is common and may be severe at times.

As the apophyseal joints of the spine are involved there is associated muscular spasm of the paravertebral muscles which tends to hold the spine straight, producing a flattening of the lumbar curve. When this muscular spasm is greater on one side of the spine than the other it will produce scoliosis. This causes limitation of motion of the spine, and tenderness to pressure or percussion over the spinous processes. Later the apophyseal joints become ankylosed, and the paravertebral ligaments calcify. At this stage frequently the back pain and tenderness lessen but the back remains stiff and rigid in a straight or kyphosed position.

One of the most common deformities is decrease of anterior posterior chest diameter, giving



Figure 1: Note 1 "Bamboo" appearance, calcified ligaments; 2 Sacroiliac ankylosis; 3 hip changes; 4 involvement of symphysis pubic; 5 changes of Ischium.

ing an anterior flat chest appearance with frequent lumbar lordosis, dorsal kyphosis with protruded head, depressed chin and ankylosed neck, the ribs being fixed in expiration as a result of costovertebral ankylosis. Chest expansion is zero or very low and breathing abdominal. This accounts for the high incidence of pulmonary infections which are so often fatal. The vital capacity of these patients is very low but this may be overcome if correct deep breathing exercises are instituted early. Attacks of intercostal neuritis as a result of intercostal nerve irritations at the foramen ovale are common.

Constitutional manifestations of weight loss, anorexia, weakness, depression, irritability, low grade fever, tachycardia, and tiredness are usually observed, as are also elevated sedimentation rate, and mild secondary anemia.

ROENTGENORGRAPHIC FINDINGS

Although the roentenographic changes of rheumatoid spondylitis are usually characteristic, the changes may not appear for several months or years after the onset of the clinical signs and symptoms. The notable changes follow the pathological course of usually appearing in the sacro-iliac joints first, to be followed in the apophyseal articulations and paraspinal ligaments. The intervertebral disks remain normal and the vertebral bodies show only secondary decalcification.

The earliest change of the sacro-iliac joints to be noted is blurring of the joint space, later followed by broken or increased densities of joint margins and mottled appearance of adjacent bone due to areas of osteoporosis and sclerosis. Occasionally there is a pseudo-widen-

ing of the joint space as a result of marginal osteoporosis. The final stage of sacro-iliac involvement is characterized by disappearance of the articular space and the presence of bilateral ankylosis and increased osteosclerosis. The bilateral sacro-iliac change is most characteristic of rheumatoid arthritis, and was found to be evident in 100% of the cases, by Boland and Pleasant (1), and others have found this to be so in approximately 98% (3, 6, 7) of their cases of sacro-ileitis. Unilateral sacro-ileitis may be due to rheumatoid spondylitis but other causes must be ruled out, ex. tuberculosis.

The characteristic changes of the apophyseal joints are blurring of the joint bases and destruction of the articular surface. There may be areas of sclerosis and osteoporosis followed by ankylosis.

Usually the joint changes are noted in advance of the calcification of the paraspinal ligaments. The calcification of these ligaments is known as syndesmophytes, (Fig. 1, 3, 4.) and gives the characteristic bamboo appearance to the spine.

In pelvic bones one may occasionally observe periosteal thickening with roughening and mottled appearance of the ischium and pubes, (Fig. 1, 2, 3) as well as involvement of the symphysis.

DIAGNOSIS

If the possibility of rheumatoid spondylitis is kept in mind, cases will be diagnosed early, remembering that x-ray evidence comes later and clinical findings usually first. Always suspect rheumatoid spondylitis in young male adults



Figure 2: Note 1 Sacroiliac ankylosis; 2 Roughening of Ischium; 3 hip changes.

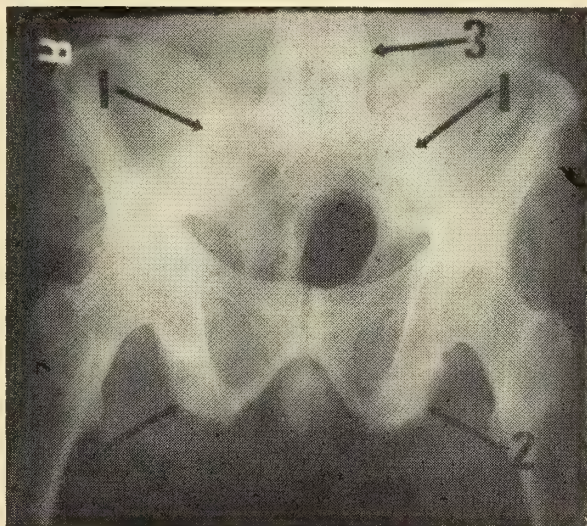


Figure 3: Note 1 Sacroiliac ankylosis; 2 Ischial changes; 3 Calcified spinal ligaments. Also involvement of symphysis pubic.

with chronic, recurrent, persistent bouts of low back, tiredness, aching, and stiffness, with or without catching pains, as well as radiculitis, whether intercostal or sciatica, particularly if initiated by sneezing, coughing, twisting, or exertion. In these early cases a low grade fever may be present, as well as a marked elevation of sedimentation rate in approximately 85% of the cases, again remembering that 15-20% of these people have a normal sedimentation rate.

The question of diagnosis is unmistakable after the disease has advanced sufficiently to produce characteristic physical and roentgenographic findings. Physical findings are those of "poker spine" and limitation of motion, paravertebral muscle spasm, absent lumbar lordosis, upper dorsal kyphosis, stiff neck with protuberant head and depressed chin, as well as flat anterior chest with very little expansion, and abdominal breathing.

X-ray evidence reveals sacro-iliac and apophyseal joint involvement, decalcification of vertebrae and calcification of spinal ligaments. However, spinal ligament calcification and unilateral sacroileitis alone are not to be considered sufficient evidence for diagnosis of rheumatoid spondylitis. These cases are for the most part easily differentiated from osteoarthritis of the spine

where osteophytes are found, and seldom confused with syndesmophytes. Here there is usually a narrowing of the intervertebral disk as well as absence of vertebral decalcification. In osteoarthritis the patient is usually past forty and the general appearance is much better than in rheumatoid spondylitis. In fact, these patients are usually overweight, fever is absent and the sedimentation rate normal. Certain specific infections, such as tuberculous sacro-ileitis, must be kept in mind, and these are usually unilateral. This alone is reason enough for careful, complete, physical examination and necessary laboratory tests, to rule in or out one or the other. In such specific spinal infections as typhoid or tuberculosis or Brucellosis, the lesion is fairly well limited roentgenographically to small sections of the vertebral column. Other conditions which may commonly simulate rheumatoid spondylitis and must be ruled out are psychogenic rheumatism, ruptured intervertebral disks, primary fibrositis and subfascial fat hernias. In these conditions the sedimentation rate is normal and the x-ray is normal except in herniated disks.

TREATMENT

There is no known cure for rheumatoid spondylitis, but early, continuous treatment of the right nature will do much to give relief of pain, prevent spinal deformity, and at times shorten the course of the disease. Symptoms are often relieved after complete ankylosis has occurred except for the limitation of motion and certain activities.

1. Orthopedic prevention of deformities is much more effective than is their correction. Much can be done by the orthopedist to relieve strain, spasm, and to prevent loss of height, kyphosis of the spine, and ankylosis of the hips. Proper beds, sleeping habits and proper braces afford much relief.

2. Physical therapy. Local heat and gentle massage increase the sense of well being, aid muscle spasm and tone, and prevent somewhat muscular atrophy and contractures. Deep breathing and postural exercises done regularly and untiringly are of the utmost importance.

3. Roentgen therapy. Many programs of x-ray therapy can be found in the literature and many excellent results have been reported. Notable improvement has been noted in as high as 70% (4, 6, 8) of the cases of some series. Repeated series may be given and improvement



Figure 4: Note 1 Bamboo Spine appearance.

usually begins in about one to two weeks after completion of the first treatments. The results are, apparently, the relief of pain and muscle spasm, as progression may be noted roentgenographically in the disease.

4. General. When foci of infection are present their removal should be advocated in order to improve the general health. Anemia, weakness, and undernutrition should be treated and improved accordingly. Fever therapy, either foreign or mechanical, may at times afford temporary relief. Vaccines are unpredictable and gold salts disappointing. Massive doses of Vitamin D have no place in the treatment of this disease.

5. Climatotherapy. Many note relief in dry warm areas, but all do not benefit by such a change.

6. Hormone therapy. The recent advent of Adrenal Cortical Hormone 17 Hydroxyl-Dehydrocorticosterone (Compound E) and Pituitary Adrenocorticotrophic Hormone (ACTH) has possibly been the greatest step in the treatment of rheumatic conditions since the advent of the salicylate drugs. In spite of the enthusiasm, there are many disadvantages to overcome in the use of these hormones. If it becomes possible to eliminate or prevent the cause of serious side reactions and still maintain the beneficial results of these compounds, many arthritics will have a brighter, more comfortable and useful life than has even been possible for them before. The exact influence that these compounds have had upon rheumatoid spondylitis has not been adequately investigated as yet.

PROGNOSIS

The extent of deformities and permanent disability depends mostly on the type of treatment the patient receives. In cases of improper care the disease usually progresses, subject to remissions and exacerbations, each exacerbation causing more deformity and the patient seldom having relief from pain until bony ankylosis has occurred. These patients are commonly left with a rigid rib cage, "poker spine", or marked kyphosis, and a variable degree of pain. This end may be reached in 5-20 years depending on the severity and velocity of the disease. However, with proper and untiring therapy many deformities can be prevented and others minimized, thereby maintaining the patient's usefulness. Rheumatoid spondylitis within itself

is not a fatal disease, nor does it usually shorten life. Death usually occurs from some concurrent infection, most often pulmonary. Complications of iritis, pleuritis, and endocarditis are more than incidental. Subcutaneous nodules may occur if peripheral joint involvement is present.

COMMENT

1. Rheumatoid spondylitis is a chronic, progressive disease characterized by variable remissions and exacerbations. With each exacerbation there is increased deformity and limitation of motion. Its course may become arrested at any stage of progression, and pain becomes less as ankylosis occurs, whether the patient's spine is straight or kyphosed.

2. To diagnose rheumatoid spondylitis early and without x-ray evidence one must be ever conscious of its frequency and clinical picture. The diagnosis is simple after the characteristic deformities and x-ray changes have occurred.

3. Successful, as well as encouraging results in treatment depend on early diagnosis as much as the correct type of therapy.

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OCCUPATIONAL DISEASES OF THE CHEST

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The reader is to understand that this article is a condensed version of the discussion of the subject given before the General Practice Symposium on Chest Diseases. It is unfortunate that this must be so, since certain omitted aspects are actually essential to a better grasp of the problem. As in the original paper, the emphasis here will be placed upon diagnosis.

In no other phase of medicine are the fundamental steps in diagnosis so ignored as they are in the conclusions reached regarding diseases of occupational origin. Physicians who will go to great end to prove a diagnosis of pulmonary tuberculosis, for instance, will assume the diagnosis of an occupational disease without adequate study or inquiry. They are too prone to accept the patient's statement that his illness is due to some type of exposure at work. This is understandable, since the average physician receives no teaching of this subject in medical school and his post-graduate courses have been largely devoid of any subject dealing with the diagnosis of the occupational diseases. Nevertheless, excusable or not, failure to accurately diagnose an occupational disease works undue hardship upon the workman suffering from or allegedly suffering from an occupational disease.

Omitting mention of several basic steps in the diagnosis of the occupational disease in general, three primary considerations concern us when we deal with affections of the lungs. The first of these is the history. It is obligatory that the patient's complete life-time employment be obtained. The physician must elicit with meticulous care each and every activity the workman has engaged in since he left school. This is especially true when it is suspected that the patient's lungs have been affected by a dust. To illustrate, a physician was at a loss to account for a considerable degree to fibrosis of the lungs as revealed by x-ray in a man whose employment history was that of an apartment house manager for 7 years, and prior to that a rancher for 4 years. Had the examining physician inquired further he would have found that the man had been a hard rock miner for 22 years, an employment which explained the pulmonary

fibrosis.

The second important step is to determine the nature of the substance alleged to have caused the pulmonary disturbance. If it is a chemical in the nature of a fume or gas, or even a dust, one must distinguish between the irritants, the asphyxiants, and the large group of volatile substances having a narcotic or anesthetic-like action. For the purpose of this article and without opportunity to explain in detail, it can be stated that most chemicals do not affect the pulmonary tissue. The irritants affect the upper respiratory tract, but the exposed victim usually withdraws from his exposure before the lungs are affected. Likewise, the asphyxiant action of carbon monoxide or the cyanides is not upon the lungs but rather the action takes place within the blood stream or upon the cells of the body tissues (internal respiration). As for the volatile drugs, they pass through the lungs to be absorbed by the blood stream and affect primarily the central nervous system.

Exceptions to the foregoing paragraph are found in such metals as cadmium oxide or beryllium, such gases as nitrogen dioxide and phosgene, and the dust, of which more subsequently.

The third important phase in diagnosis is the utilization and interpretation of the x-ray films. Herein lies the chief diagnostic pitfall. Today the x-ray machine is as ubiquitous in the average physician's office as it diathermy. It is reasonable to assume that for the purpose of determining a fracture or the presence of a foreign body only ordinary acumen is necessary. This is not true in the case of the interpretation of chest x-ray films. It is especially true that probably no phase of roentgenographic interpretation is as inaccurate as that of the chest films of industrial workers. There seems to be a universal tendency on the part of the inexperienced physician to read into chest films of those exposed to dust or chemicals a pathology which is not actually present. A few scattered, old nodules or a minimal increase of the perivascular markings in a housewife would be accepted on their historical face value, but in the industrial worker they are too often given unwarranted emphasis. This misinterpretation will force a workman to withdraw from a job which is not only re-

munerative but which was attained only after long years of labor. Also it ill cause him to live under a cloud of apprehension. On previous occasions and in other articles I have quoted Pancoast. It is just as timely to do so here. He once remarked, "Let's not talk about the normal chest. We probably see normal chests only in children. Let us speak about the healthy chest."

Concerning the dusts an unfortunate situation exists in that many years ago the term pneumoconiosis was introduced. With the passage of time the suffix "osis" conjured up in the minds of many physicians the disease known as silicosis, so that today there exists a failure to distinguish between a benign pneumoconiosis and that condition which results in a disabling fibrosis of the lungs. The distinction between a disabling and a non-disabling fibrosis deserves our utmost consideration.

Before considering the nature of a dust it is necessary to recall the protective mechanism that nature endowed man with in order to prevent the inhalation of dust. Man lives in a konispherea world of dust. His first and his last breath contain dust. Therefore, were it not for the hair of the nose, the moisture of the nasal membrane, the ciliated epithelium of the trachea, and the hilar lymph nodes, dust would invade the lungs. Even so, because of the absence of chemical reaction most of it is incapable of setting up any proliferative reaction and remains inert or is passed out of the respiratory system.

Other factors often ignored in the consideration of industrial dusts are those of weight, particle size, concentration, and chemical nature. It must be appreciated that for a dust to be inhaled it must be extremely light, so light that it will float or remain suspended in the breathing zone of the exposed worker. It must be of minute particle size and highly concentrated. Failing to meet such qualifications, the average dust does not enter the pulmonary field.

Space forbids a detailed consideration of a number of common inert dusts such as iron dust, cement dust, fiberglas, coal dust, dust from grinding or abrasive dusts, wood dust, etc. For instance the inhalation of iron dust over a period of 8 or more years may produce a condition known as siderosis. Unfortunately the term and the x-ray markings have been confused with silicosis, an entirely different patho-

logic entity. Siderosis is a benign condition characterized by round, sharply defined opacities which result from pigmentation of the iron. No reactive fibrosis occurs, the condition by x-ray remains the same for life, and does not progress to confluent nodulation or impairment of respiratory function. The staining of the lung surface due to the iron pigment is as harmless as the tattooed nude on a sailor's chest.

Cement dust is another example of an inert dust. For some years I have examined the workers of a cement industry in this area and review annual x-ray films of these workers. These men fail to evidence any clinical signs or symptoms of pulmonary disturbance due to dust and the films remain negative even after as many as 30 years of exposure, except in a few instances of a minimal fibrosis. Furthermore, my experience is in keeping with that of the Saranac group. (1) (3).

"The Saranac Laboratory, under the guidance of the late Leroy Gardner, conducted in 1935 a survey among cement workers which was reported in its entirety in 1939. Over two thousand workers were examined, 70 per cent of whom had been employed for periods varying from ten to fifty years. Of the roentgenograms, 82.06 per cent showed no abnormalities of any kind, 17 per cent revealed a certain degree of linear exaggeration. Further analysis indicated that about one-half of this group had been exposed to dusts other than cement prior to being employed in the cement industry. No nodulations were seen in the films of those workers who had been exposed only to cement dust."

"Fiberglas (wool glass, mineral wool, etc.) is a comparatively recent industrial product and information regarding its action upon the lungs has not yet found its way into the general medical literature. The name and the physical appearance of this substance are such as to lead workers and physicians to believe that it is bound to be harmful to the lungs. Chemically, this material contains no free silica and its physical characteristics render it non-respirable. Because of the impression created by early erroneous ideas, about the harmfulness of fiberglas, extensive animal experimentation was carried out and numerous surveys of exposed men were conducted. These all

revealed no evidence of pulmonary damage."

In previous publications additional inert dusts were given consideration, but these must be ignored at this time. Suffice it to state that except for free silica dust and a few of the silicates, all industrial dusts cause *no disabling fibrosis* of the lungs. This fact is as scientifically established as the fact that pulmonary tuberculosis is not caused by the typhoid bacillus.

The untutored physician is not usually cognizant of the difference between free silica and the silicates. The explanation involves a chemical appreciation of crystallization of the "primary minerals". Silica, SiO_2 , is composed of silicate tetrahedra, SiO_4 —, a structural unit which was first revealed by x-ray. In studying the internal structure of crystals, among other things it was noted that separate SiO_4 — tetrahedra alternate in the space lattice with positively charged metallic ions in certain silicates, while others are linked together in pairs, with an oxygen ion in common. "Since each oxygen ion is shared between two different silicate tetrahedra, there are only half as many oxygen ions in the complete solid structure as the formula SiO_4 — would seem to suggest; in other words, the formula of the solid structure, extended indefinitely in three dimensions of space, is a triple infinite multiple of SiO_2 ". However, the chemistry of the silicates is not so simple as the foregoing would indicate, owing to the arrangement of the oxygen ions in the structure, for some groups possess oxygen ions which are not linked with other groups, while two ions may be shared with other groups. A chain, for instance, of infinite multiples of SiO_3 may be formed. The fibrous structure of asbestos is due to the linking of silicate groups in continuous chains.

The silicates are abundant in industry, whereas pure silica is less so. In the silicates, the silica is bound by the chemical structure so that it is not released to act as a harmful agent to the lungs. One should always differentiate between a hazard in which silica as such is present and one in which the silica is locked within the chemical structure of the silicates and is, therefore, inert. This fact must be kept in mind when one reads a chemical analysis of a substance which shows the presence of a high content of silicates, but does not reveal the actual content of the silica as such in the mineral. In fact, a chemical analysis of a material is not

satisfactory for the determination of the exact percentage of silica present.

Within the past several years we have learned that a few of the silicates when subjected to high temperatures convert the "locked up silica" or amorphous silicic acid to a cristobalite, or in some instances tridymite, forms of silica capable of producing a disabling fibrosis. Bauxite, hydrous aluminum oxide, is an example of this conversion as is diatomaceous earth. In the original (3) paper the peculiar aspects of beryllium were discussed and x-ray films were shown. This cannot be done here.

Silicosis is a disease of the lungs resulting from years of inhalation of dust containing free silica and characterized by nodulation and fibrosis. The disease is progressive. The serial films of a given case will reveal beading along the perivascular markings, diffuse nodulation, fibrosis, subsequent confluence of the nodules, especially in the upper lung fields, increase of the fibrosis and frequently the complication of tuberculosis. A few scattered nodules are not indicative of silicosis. The differential diagnosis must consider sarcoidosis, histoplasmosis, miliary tuberculosis, coccidiosis, or old primary tuberculosis. Clinically the silicotic complains of dyspnea, cough, and fatigue. The history of prolonged exposure to free silica dust, the aforementioned symptoms, and the x-ray findings of diffuse, varied-size nodulation and marked fibrosis clinch the diagnosis.

Conclusions:

1. The diagnosis of pulmonary affections due to occupational exposure involves primarily a good work history, an evaluation of the alleged offending substances and intelligent interpretation of the x-ray films.
2. The majority of all fumes, gases, vapors, or dust do not affect the lungs.
3. Concerning the dusts, it is necessary to distinguish between those which are relatively inert and those which may cause a disabling fibrosis.
4. X-ray evidence of fibrosis should not be interpreted as indicating disability. The majority of all adults have some degree of pulmonary fibrosis. It is only when the degree becomes marked that disability is to be accepted. Nodulation or pigmentation is not in itself disabling.

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PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL HOSPITAL CASE NO. 29152

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A sixty-seven-year-old school principal entered the hospital because of loss of weight and strength.

Nine months before entry the patient noted the onset of nausea with occasional vomiting after breakfast. At the same time he developed a "bronchial" cough productive of small amounts of whitish non bloody sputum. This lasted two or three weeks, and two similar episodes occurred in the two following months. The paroxysms of cough were preceded by a tickling sensation in the throat, which he attributed to a large goiter that he had had for twenty-five years. There was no dysphagia. X-ray films taken by his physician were said to have shown four small gallstones and cloudiness at the apex of the right lung. He had been taking bile salts with some relief. During the four or five months before entry he became aware of progressive loss of strength and easy fatigue not relieved by rest. His appetite was poor, and he had lost thirty-eight pounds in weight during the previous two months. Because of mid-afternoon fever of 99 to 100°F., he remained in bed for two months prior to entry. Many specimens of sputum were negative for tubercle bacilli. Three weeks before admission the patient had his first attack of rapid pulse, the rate rising to 150, with associated headache and faintness. Since then he had three similar attacks, each beginning without warning and relieved by pressure on the eyeballs or carotid sinus.

He had had left-sided pleurisy twenty-five years previously, and pneumonia on the right and a suprapubic prostatectomy five years before entry. The family history was noncontributory.

Physical examination showed a well-developed but emaciated man with a dry and pale skin. There was a large, nodular, firm, but not stony-

hard, tumor of the right lobe of the thyroid gland, which extended laterally beneath the sternocleidomastoid muscle and substernally. The trachea was deviated to the left. Examination of the heart and lungs was negative. The abdomen was slightly distended; in the right upper quadrant there was a definite sense of resistance and dullness but no well-defined border could be made out. The right kidney was movable, firm nontender and neither enlarged nor displaced; the left was not palpable. Rectal examination was negative.

The blood pressure was 100 systolic, 45 diastolic. The temperature was 100°F., the pulse 90, and the respirations 20.

Examination of the blood showed a hemoglobin of 8.2 gm. and a white-cell count of 12,100 with 81 per cent polymorphonuclear neutrophils. The urine was cloudy and amber, had a specific gravity of 1.020 and gave a two plus test for albumin; the sediment contained a few red cells and many white cells. The stools were negative. A blood Hinton test was negative. The serum nonprotein nitrogen was 23 mg. per 100 c.c. A sputum examination was negative for acid-fast bacilli.

An x-ray film of the chest showed numerous areas of calcification in the region of the right middle lobe. There was scarring in the right upper lobe. A mass at the base of the right neck with calcification in its walls displaced the trachea sharply to the left and extended slightly into the chest.

By x-ray the left kidney had a normal outline. The right kidney was enlarged and there appeared to be a definite bulge with some lobulation along the lateral surface. No stones were seen. An intravenous pyelogram showed prompt excretion of the dye on the left, which outlined normal urinary passages. The middle calyces on the right were displaced medially and showed evidence of pressure defects without invasion. A retrograde pyelogram showed only partial filling of the right middle calyx.

Cystoscopy showed only a small amount of urine in the bladder. The flow of urine was extremely slight; at first the right ureter drained hazy urine followed by very bloody urine, and the left cloudy urine.

On the seventh day the white-cell count was 31,900. The temperature fluctuated between 99 and 101.2°F. Two days later an operation was performed.

DR. W. WARNER WATKINS

Sixty-seven years old! Just my age, which suggests that this unfortunate old gent might be afflicted with geriatric problems, for which solicitous friends would prescribe "Four Roses", either to smell or drink, depending on personal idiosyncrasies or former mode of life.

Apparently he has kept out of the clutches of doctors to a large degree, but not entirely so. He had a left side pleurisy 25 years ago, and five years back he had a prostatectomy and pneumonia, tho stated in reverse order in the history. Elsewhere in the record a thyroid enlargement is mentioned as dating back 25 years, apparently not bothering him very much.

Four years and a few months after the prostatectomy, the old man began to go to pieces. Nausea and vomiting after breakfast, without mention of Four Roses as a cause; three spells of so-called bronchial cough, with gallstones and cloudiness at right apex shown by x-ray; progressive loss of weight and strength, poor appetite, slight fever,—all of which kept him bedfast for the two months immediately preceding entry to the hospital. These symptoms, with sputum negative for tubercle bacilli and three attacks of tachycardia, apparently of idiopathic type,—make up the background of this case.

I felt a yen to go back to an old technic of analyzing these cases in three steps:—

First Step—On the basis of the history up to the time of the present illness, list all the possibilities suggested by these data, by classes and not by specific diseases. Chief among these would be,—

Malignancy somewhere,—either primary or secondary.

Chronic or recurrent infection,—of some type, somewhere.

Degenerative diseases of the aging,—such as chronic kidney disease, cardiovascular disease, liver degenerations, central nervous system disease.

Blood diseases,—aplastic anemia, pernicious anemia, Hodgkin's disease, and so forth.

Primary diseases of lungs, heart, digestive tract, liver, kidneys, brain.

With this list before us, and not pretending that it is comprehensive, we pass on to the—

Second Step—This is the physical examination, and the question whether it eliminates any of the above-mentioned possibilities, or adds

new ones. The physical examination found the heart and lungs negative, which will require checking by x-ray; a thyroid tumor, on right side, large, firm and nodular; abdomen slightly distended with resistance in upper segment; movable, non-tender right kidney on right, not enlarged to palpation; low blood pressure, some fever, pulse rate up somewhat.

So, what? Apparently the examiners were not greatly impressed by some of the possibilities suggested by the history. Since they had the patient under their eyes, we will defer to their judgment and delete most of the degenerations mentioned,—except possibly chronic kidney disease. We still have the malignancies, chronic infections, blood diseases and local diseases of important organs to carry with us to the—

Third Step—What do the clinical laboratory tests and x-ray examinations indicate, by way of deletion of or addition to, the possibilities? The hemoglobin of 8.2 indicates an anemia, but evidently the examiners did not give serious thought to any of the fancy blood diseases,—so we will follow their leading and forget these. Apparently there was a pyuria, so we keep the kidneys high on the list of possibilities. The normal NPN would seem to exclude any advanced chronic nephritis.

We will look at the x-rays. The chest film shows calcifications on the left which may date back to the infection with pleurisy 25 years ago. Many people develop tuberculous infection with pleurisy, recover from it and show calcification or other scarring many years later. Our x-ray survey will disclose hundreds of these, no doubt. The lobulated shadow in the region of the right middle lobe with calcification and scarring in the right upper lobe may all be one with the old left side shadows. Since this patient has two known possible sources for a metastatic malignancy, this lobulated shadow becomes important in differential diagnosis. The old nodular goitre could finally become malignant and metastasize to the lungs; the prostate removed four years back might have been malignant. With regard to the lung shadow, it is important to know its size, whether it is sharply defined or hazy at the margins, and whether the calcification is actually in it, or merely superimposed upon it on the film. Calcification can occur in other lesions besides tuberculosis, but the burden of proof would be on any one who would regard a calcifying

lesions in the lungs as anything else than tuberculosis. On the basis of the roentgenographic findings as described, therefore, the shadows would be interpreted as old tuberculosis until proven otherwise, and probably not the cause of serious symptoms. No mention is made of cardiac or aortic enlargement, so we will remove cardiovascular and active pulmonary diseases from our list,—and move downstairs.

Plain film of the abdomen showed normal size and contour of the left kidney. The right kidney is enlarged, contrary to the impression on palpation,—and shows a lobulated bulging on its lateral border. By intravenous visualization, the left kidney appears normal. On the right the middle calyces are displaced medially, so that we can safely interpret some sort of space filling lesion in the right kidney cortex, pushing out in both directions from its place of origin. The retrograde check confirmed these findings of pressure defect at area of middle calyx. The description of the urine obtained by cystoscopy is not adequate; it is said that the right ureter drained "hazy" urine and the left "cloudy" urine; what these distinctions signify is not certain. Later the right ureter drained very bloody urine. Then the white count jumped to 30,000 and the temperature rose,—and the surgeons took over.

It seems, therefore, that we have narrowed the location of the trouble down to the right kidney, and the possibilities to neoplasm or infection, or both.

Two types of neoplasm and two types of infection require consideration. Tuberculosis has to be ruled out, and we will just assume that this was done. Cortical abscess of chronic type leaking into the kidney pelvis cannot be excluded on the basis of information given. Hypernephroma or renal carcinoma of smooth or cystic type ranks high among the possibilities, and a close second would be renal cyst with complicating pyelonephritis. Time does not permit a review or analytical discussion of these possibilities, but a brief comment on cyst of the kidney will be pertinent. Several remote possibilities I cannot discuss at all, such as the metastatic lesions from thyroid or prostate.

A recent paper by Ochsner on "Cysts of the Kidney" offered some pertinent observations, among which are,—

The diagnosis is usually missed by urologist and radiologist.

They are frequent in the fifth and sixth decades.

While most frequent at the kidney poles, they are also observed in the central portion of kidney.

There is frequently a concomitant urinary tract infection.

There may be a rounded shadow merging with the kidney outline.

Deformities of the calyces in the pyelograms include displacement, flattening, abbreviation, obliteration.

Hemorrhagic cysts are sometimes found; they do not project like serous cysts and are continuous with the contour of the kidney surface. In one of Ochsner's patients with a hemorrhagic cyst the symptoms included pain in flank, nausea and vomiting a few weeks before admission, gross hematuria and a renal mass, weakness and a moderately severe urinary tract infection.

Calycine or peripelvic cysts are small cortical cavities which communicate with a minor calyx and are situated just distal to the calyces; they may be multiple or single and up to 2.5 cms. in diameter; they bulge beyond the lateral margin of the kidney.

The differential diagnosis between calycine, hemorrhagic or serous cyst with concomitant infection, cortical abscess associated with chronic pyelonephritis, and hypernephroma, is said by this writer to be difficult and often impossible. Apparently, we are expected to do the impossible in this case.

The suggestions which favor hypernephroma (carcinoma) of smooth or cystic type,—are, right age range; consistent x-ray findings, profound and progressive general effects such as loss of weight and strength, and anemia, upper abdominal symptoms which could be due to metastatic spread to liver or retroperitoneal lymph nodes, and possible lung metastasis.

Favoring cortical abscess or cyst with infection are,—long duration, the leucocytosis, the bulging both ways of a renal cortex lesion, the smooth surface contour, the pyuria.

Dabney Kerr, in discussing Ochsner's paper, emphasized the difficulty in making this differentiation from either roentgenologic or clinical findings. He said,—“It is practically impossible to tell with certainty whether one is dealing with a simple cyst or with a cystic type of renal neoplasm. . . . We work on the assumption that if there is a question regarding the identity of a

mass in the kidney, whether or not it might be a neoplasm, it must be considered a surgical problem and the patient explored and almost certainly the kidney removed."

As a practicing radiologist, I would like to climb onto that safe platform with Dr. Kerr, and pass the buck to the urologic surgeon. However, in this Club, the cervical spine is supposed to be extended into a non-retractable stance and laid cheerfully on the guillotine. Yielding to this merciless rule, I will spread my bets as follows:—

FIRST CHOICE:—Malignant neoplasm of right kidney,—hypernephroma or renal carcinoma of cystic type, with metastases to liver and retroperitoneal lymph nodes,—possibly to right lung.

SECOND CHOICE:—Cyst of kidney, calyceine or hemorrhagic, with pyelonephritis.

THIRD CHOICE:—Chronic abscess of kidney cortex.

DIFFERENTIAL DIAGNOSIS

Dr. Fletcher H. Colby: It seems to me that the significant history starts with the statement that the patient became aware of progressive loss of strength and easy fatigue not relieved by rest. He also had a low-grade midafternoon fever during that time. There were episodes of rapid pulse, which I imagine were attacks of paroxysmal tachycardia associated with the enlarged thyroid gland.

On physical examination the patient gave evidence of considerable loss of weight and strength. The mass in the neck was obvious, and from the history the patient had had this mass for twenty-five years. I assume that it probably was a colloid goiter. Although there is a possibility of malignant change, the fact that the patient had had this goiter for twenty-five years makes it seem improbable. The other essential points in the physical examination are the suspicion of a mass in the right upper quadrant, the pus in the urine and the confirmation by x-ray examination that there was a mass in the right upper quadrant. X-ray examination also showed an enlarged kidney, and this is certainly better evidence of enlargement of the kidney than physical examination, because we all know how large kidneys can be and yet be missed on palpation. The intravenous pyelogram suggests trouble in the right kidney. The left kidney was interpreted as normal. This suspicion of abnormality on the right seem to be confirmed

by the cystoscopic examination, when a retrograde pyelogram made of the right kidney showed that the middle calyces were displaced medially with a pressure defect and without evidence of invasion of the calyces. So I believe that the important thing to consider in this patient is the right kidney. The evidence suggests that the mass was intrinsic in the kidney itself. The kidney outline was well known by x-ray examination and appeared to be irregular, with a definite bulge. The retrograde pyelogram indicates that this mass involved the middle portion of the kidney and displaced the middle calyx. So I think the diagnosis comes down to disease within the kidney itself. The possibility of perirenal infection seems to be eliminated. This mass on the right side, presumably the right kidney, was nontender, and one would expect perirenal infection to give tenderness.

Dr. Holmes will you be kind enough to interpret the x-ray films?

Dr. George W. Holmes: I think I had better discuss the chest film first. The mass that is described is quite evident. It lies in the upper part of the anterior mediastinum in the region of the thyroid gland and contains calcium. So the only other things we have to think of are parathyroid tumor and a calcified tuberculous node. The position is very much against the latter. The findings in the lungs are more suggestive of tuberculosis than of anything else. There is one round shadow that might be a metastasis from a tumor.

Dr. Colby: That is the one with the fairly sharp edge?

Dr. Holmes: Yes; it is not quite so dense as one would expect it to be if it were old tuberculosis.

Dr. Colby: Calcification is described in that mass. Could it not be calcification somewhere else?

Dr. Holmes: It is not impossible for a tumor to show calcification. So I cannot state whether the shadow was due to tumor or to old tuberculosis. I do not see how one can connect it with the shadow in the neck.

Dr. Colby: The calcification in the neck is probably in the thyroid or parathyroid.

Dr. Holmes: I should think that was most likely because of the position. If the calcification was in a tuberculous node, the mass ought to lie alongside the trachea or up in the neck

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SEARLE

RESEARCH IN THE SERVICE OF MEDICINE

WHEN WRITING ADVERTISERS PLEASE MENTION THIS JOURNAL

itself.

In the abdominal films there is a definitely enlarged right-kidney shadow. The lobulation is not so evident as one might expect from the notes, but I think it is present. The outline of the kidney is sharp, which is against an inflammatory lesion. In an inflammatory lesion, one usually does not visualize the kidney so well. The calyces, although displaced, are not irregular, which again is against an inflammatory lesion. It apparently is deep in the substance of the kidney, so that it pushes the calyces outward, and in all probability it is some sort of tumor. I doubt that a cyst would be in this position, and I shall be surprised if it turns out to be inflammatory. The density does not give a lead.

Dr. Colby: I think it is fair to say we come to the diagnosis of an intrinsic lesion of the right kidney. This could be either inflammatory or neoplastic.

What are the possibilities of an inflammatory lesion? First of all, a cortical abscess of the kidney should be considered. This is usually associated with preceding infection, which is possible in this patient, since he had had a low-grade fever for several months. However, he should have had backache and pain and he should have had tenderness. The pyelograms in such cases vary. My experience has been that with a cortical abscess there is a definite pressure defect, either of the kidney pelvis or, more often, of the calyces themselves. The calyces are usually compressed in a somewhat orderly fashion, and one does not see the irregular defects that are apt to be associated with tumor. So I do not believe this is a cortical abscess because of the lack of tenderness, the lack of pain, the lack of backache and the pyelographic evidence.

The only other inflammatory condition I can think of as a possibility is tuberculosis. The patient's age is against tuberculosis. Patients as old as this rarely have primary renal tuberculosis unless there is a definite past history of other lesions. That does not make it impossible. However, the patient apparently had had no bladder symptoms, and an irritated bladder is the most frequent symptom of renal tuberculosis. No ulceration or inflammatory change was described in the bladder on cystoscopic examination. Furthermore, the pyelogram was not consistent with tuberculosis. One would ex-

pect to find tuberculosis in more than one portion of the kidney, and as Dr. Holmes described the pyelogram it does not suggest an inflammatory lesion.

So far as neoplasm is concerned, what is the possibility of metastatic malignant disease? The thyroid gland might have undergone malignant change, but I do not believe so, and I am going to discount that. Primary tuberculosis of the thyroid gland is rare, and if it occurs, is usually associated with miliary disease in general. Is that not true, Dr. Holmes?

Dr. Holmes: Yes.

Dr. Colby: At the Lakeville Hospital we have had only a few patients with tuberculosis of the thyroid gland.

The possibility of primary lung tumor that metastasized to the kidney should be mentioned. However, there is no real evidence that this patient had a primary carcinoma of the lung. In addition, the other systems give no lead to a primary tumor that might have metastasized to the kidney.

So we come down to the possibility of primary malignant tumor in this patient's right kidney. He had fever, weakness and loss of strength, and in our experience at this hospital these are evidence of malignant neoplastic disease somewhere. Although there is no convincing evidence of symptoms such as pain, hematuria and tumor, which are the three cardinal signs of renal tumor, these have long since been discarded as early indications of neoplasm. I cannot explain the fever except to say that it was evidence of infection. The well-marked anemia and the white-cell count of 31,000 after cystoscopic examination could have been due to the flaring up of an already present infection in the urinary tract. The kidney outline was suggestive of neoplasm, and the pyelogram indicated a tumor that involved the middle portion of the kidney. The area in the chest might have been a secondary deposit from a tumor of the kidney.

My diagnosis is a primary malignant tumor of the right kidney; and most of these tumors are renal-cell carcinomas.

CLINICAL DIAGNOSIS

Carcinoma of kidney.

DR. COLBY'S DIAGNOSIS

Primary malignant tumor of right kidney.

ANATOMICAL DIAGNOSIS

Undifferentiated carcinoma of right kidney.

PATHOLOGICAL DISCUSSION

Dr. Benjamin Castleman: At operation a large tumor (9 by 6 by 4 cm.) of the right kidney was found, which proved on section to involve most of the midportion of the kidney. The tumor was yellowish and necrotic, and microscopically shows an undifferentiated carcinoma, probably of embryonal origin. There

was no invasion of the renal vein or pelvis, although the latter was displaced by the tumor.

Dr. Colby: Does anyone know anything about the nodule in the chest?

Dr. Castleman: No. The calcification in the neck might well have been a colloid goiter; many of them have some areas of calcification.

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

Editorial

PRE-ANESTHETIC PREPARATION AND ANESTHETIC MANAGEMENT IN THE AGED

It is apparently quite true that the number of our Senior Citizens is increasing from year to year. You are all aware of this, I am sure; but a few figures may give you a better appreciation:

In 1900 one person in 25 was 65 or over.

In 1940 on person in 14 was 65 or over.

The 1950 census revealed that approximately 11½ million people in the United States are over 65. At the present rate, there will be 20 million over 65 in 1975, and 31 million over 60 years of age. There is no doubt, then, but that we shall have to concern ourselves more and more with the problems of the aged. This portion of the discussion is concerned with pre-anesthetic preparation and anesthetic management of this group.

In the pre-operative consideration of the patient, we must realize that there are certain physiologic changes which occur with increasing age. These changes occur at varying rates in different individuals. Thus, while one man's lungs may be functioning perfectly, his heart may not be. Another's heart may be as perfect as that of a healthy 30-year-old, but he may have serious nephritic o rhepatic changes. Let us consider, then, how the various systems may be involved in the physiologic changes of age, and how these changes may complicate anesthesia.

In the circulatory system any of the following may exist: Cardiac hypertrophy, diminished caliber and elasticity of the coronary vessels, arterio-sclerotic changes in all the vessels, or myocardial degeneration of varying degrees. We must expect a decreased cardiac reserve and watch for hypertension, heart failure, and a sluggish circulation. Coronary occlusion can be precipitated in the operating room. Faulty conduct of anesthesia may also result in thrombosis or

embolic phenomena. As examples, we may mention the danger of giving high spinals to patients with coronary artery disease and administering intravenous fluids indiscriminately to patients with relative or true polycythemia.

In the respiratory system there is usually a stiffening of the thoracic cage, atrophy of the mucous membranes of the upper respiratory tract, calcification of the cartilages, dilatation of alveoli and rupture of interalveolar septa, emphysema, and narrowing of bronchioles. With these changes there is a decreased tidal volume and vital capacity and impaired gaseous exchange through the alveolar membrane. Elimination of secretions from the respiratory tract is sluggish. The overall effect of pulmonary ageing is a state bordering on chronic hypoxia.

In the nervous system atrophy and degeneration of the cortical elements may occur, and because of this many physicians prefer atropine to scopolamine in the premedicating hypodermic. Reflexes may be diminished and sensations impaired.

Ageing of the gastro-intestinal tract and excretory mechanisms results in delayed absorption and elimination of certain anesthetic agents.

Any number of these changes may be present, or none to any serious extent. The important thing is to understand and recognize the physiologic changes of age and know how to cope with them.

This brings us to a consideration of actual anesthetic management, which may be divided into two equally important periods: Pre-operative and operative. Perhaps the most important factor in pre-operative management of the patient is a visit with him on the evening before surgery. He knows and has confidence in his surgeon, but probably has little or no idea as to anesthetist or anesthetic. And he may be reluctant to ask his surgeon about the anesthetic, lest this be interpreted as a sign of fear. With a few well-chosen words the anesthetist can often put the patient completely at ease and give him a good night's rest.

Other important things can also be accomplished at the time of the pre-operative visit: The pre-operative medication can be ordered. The choice of drugs and determination of dosage are matters of individual preference, but most anesthetists will agree that it is a mistake to apply routine adult dosages to the aged. This is readily appreciated when it is remembered

that the metabolic rate in these patients is often greatly reduced. Circulatory collapse from heavy pre-medication is not uncommon and is occasionally of such severity as to require postponement of surgery. There is considerable agreement that too little premedication is to be preferred to too much, for more can be added but none can be taken away.

Also at the time of the pre-operative visit certain pathological states may be recognized and corrected. Anemia, dehydration, and vitamin and mineral deficiencies should be looked for and treated. Digitalis is indicated pre-operatively in patients with congestive failure, and insulin for diabetics with a blood sugar greater than 150 mgm/100 cc. One must know when to suspect the presence of such obscure diseases as Addison's, myasthenia gravis, and multiple sclerosis; and more common pathological conditions such as asthma must be considered and inquired about. If the patient is an asthmatic, the anesthetist must be prepared for quick and effective treatment of an acute attack in the operating room.

Anesthetic management during surgery, again, is very much a matter of individual preference. The choice of agent is usually governed by the need for adequate oxygenation and the preservation of an active cough reflex. Any agent known to cause prolonged post-operative respiratory depression is contraindicated from the standpoint of increased incidence of atelectasis and pneumonia. If these few precautions are heeded, one may rightfully expect the older patient to tolerate both surgical procedure and anesthesia quite well.

In summary, then, we must prepare to deal with all the varying physiological and pathological states of the aged. The anesthetist can fulfill his part best by making pre-operative contact with the patient and following the path indicated by correct evaluation of that particular individual.

W.A.R.



TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER, M.D.

The ANTIBIOTICS have accidentally produced some odd, unfortunate situations. Part of the fault is in their use, part in the way they are used. . . . For example, a group from Duke University has reported two dozen cases of MONILIASIS—an infection of various body areas and portals which was allowed to occur because the usual bacterial flora was killed off. . . . A Los Angeles surgeon has reported the masking effect which penicillin may have on appendicitis . . . Etc., etc.

Furthermore, an editor of ARIZONA MEDICINE (W. H. Oatway, Jr.) has just won the yearly award of the California Trudeau Society (\$150) for a paper entitled "DELAYS OF THE DIAGNOSIS OF TUBERCULOSIS FROM THE INCAUTIOUS USE OF ANTIBIOTICS". . . . Forty per cent of the present population of a small sanatorium were held up for weeks to years in their start of tuberculosis therapy. Chemotherapy was used for lung symptoms, called by a variety of 'virus' names. From one to five different drugs were used, often in sequence. Chest x-rays and bacterial studies were not done when indicated. About half of the group were finally found by an incidental 'survey' x-ray. Another goodly portion had been known to have tuberculosis for years, but the antibiotics were tried for weeks or months before the activity of the lung lesion was determined. . . . The report is a good warning on the need for diagnosis, and the value of survey films and fluoroscopy.

About two years ago the regular reduction in the cost of new drugs was described in this column. . . . Merck & Co., Inc. have recently added another proof of super-honest pharmacy. Right in the midst of a CORTISONE black-market, Merck REDUCED THE COST of Cortone for the seventh time in two years. Not cheap yet, but \$200 to \$24 is quite a decrease.

After waiting for months to hear of local TREATMENT for A-bomb BURNS, the first program turned up within a week after the hope was mentioned in print. Col. W. S. Stone, head of the Army Graduate Medical School described it in an interview. . . . It is intended to separate the cases into two groups,—one group will include those with less than 20% of the body involved by second degree burns; the other group includes those with more than 20% of the body area burned seriously. . . . Each group will receive a particular routine of treatment. The minimal group needs only the 'open treatment'; no dressings will be applied, narcotics or analgesics may be used, and antibiotics can, be used if infection threatens. . . . The badly burned group is to be treated

by application of large pressure rolls, 2 inches thick, 22 inches wide, and 30 inches long. They are composed of layers of gauze (inside), cotton batting, wood pulp cotton, and water-repellent paper (on the outside). It was developed by co-operation between the Army, Cook County Hospital of Chicago, and the Medical College of Virginia. . . . Third degree burns no larger than an inch will heal over by themselves; larger burns usually will need skin grafts.

Another reference seems indicated to a medical celebrity in Phoenix. Dr. Milton H. Erickson, neuropsychologist, has written the foreword for the LeCron and Bordeaux book on 'HYPNOTISM TODAY', second edition.

ULCER THERAPY NO. 1—A combination of antacids (aluminum hydroxide and magnesium trisilicate), water-soluble chlorophyll, and powdered okra is recommended for resistant peptic ulcers. . . . It is called 'Chloresium Powder', and is supposed to produce symptomatic relief and tissue repair. The okra makes the material very viscid and adherent. It is made by the Ryston Co. of New York.

ULCER THERAPY NO. 2—Capsules of 'Kutrol' are used to stimulate healing of peptic ulcers. . . . They contain an extract of equine pregnancy urine, including non-estrogenic factors. . . . It is combined with other methods at the start of therapy. . . . Parke, Davis & Company makes it.

ULCER THERAPY NO. 3—The literature is piling up from the use of 'Banthine'. The drug is anticholinergic, and controls the parasympathonia which usually is present with ulceration. It reduces the hypermotility and hyperacidity. . . . The side-effects are said to be moderate and often decrease with use of the drug.

NO. 4—Dr. Walter Palmer, professor of Medicine at Chicago, feels that the value of BANTHINE has been exaggerated. No drug on the horizon does more than supplement the old remedies. . . . If suppression of secretions is needed, Dr. Palmer favors vagotomy (but only for duodenal ulcers). . . . He tells of the adverse effects of ACTH on peptic ulcers, contrary to its salutary effect on ulcerative colitis.

OKRA, incidentally, has been found to be a source of 'okra plasma', a BLOOD PLASMA SUBSTITUTE. . . . Zeit, Benjamin, and Ihrig of Marquette, in Milwaukee, have found that okra

Pods may be extracted to produce a liquid which is said to be well tolerated, and which may be obtained in powder form. . . . Storage of the powder is a great space-saver, and the last minute addition of saline solution allows its emergency use. . . . The material is a polysaccharide. It is not yet licensed for human use by the Pure Food and Drug Administration.

Transparent adhesive may come to the place where someone in 1960 will invent an OPAQUE ADHESIVE TAPE so that we CAN'T see the lesions.

The RESINS have moved from violins to industry to medicine. They have barely been started as antacids for peptic ulcer, before being recommended for REDUCING EDEMA. They start off in a fairly public way in an article in the Sat. Eve. Post. . . . The resins to be used for edema obtain their effect by desalting the alimentary tract. They attract certain ions, notably sodium and potassium, and increase the effect (and tolerability) of a low-salt diet. . . . The hazards of acidosis and hypopotassemia must be considered, but one of the drug houses already has put out a resin loaded with potassium to avoid the removal of too much from the intestinal tract.

For those physicians whose specialties do not lead them to peer into the abdomen thru a peritoneoscope, the mention of a 'CULDOSCOPE' may be news. . . . It appears (or seems) that there is a cystoscope-like instrument which may be inserted by vagina, thru the barrier of the vault and peritoneum, and into the cul de sac. . . . This allows direct visualization of the female pelvic structures. . . . It is called the Decker Culdoscope, and is made by the American Cystoscope Makers, Inc.

Big Deal! The Scherer Company announces their NEEDLELESS HYPODERMIC INJECTOR to the profession, so that we will know about it before the hoi-polloi. The same day the same information appeared in the papers. Oh, well, maybe we got it before TIME Magazine. . . . Also, unless we move to Summit or Stark County in Ohio (where it is first being sold) the 'Hypospray' will not be available for perhaps a year. . . . The spring-activated plunger forces a tiny spray of medication to a certain planned depth with scanty pain, it says here. The newspaper states that the width of the spray is 1/20th of diameter of a hypodermic needle. . . . E. R. Squibb & Sons is supplying antibiotics, biologicals, hormones, sedatives, vitamins, etc., in 'Hypofils'. . . . This slow distribution may produce an 'intrigue of scarcity', but it also may produce a series large enough for the deprived to decide if it is valuable.

The use of 'AMPINS' for hypodermic injection

of medications has been noted in advertising, and now in medical reports. Batterman and Rovensine of New York have described the values and hazards. . . . An ampin is a disposable unit which consists of a glass ampule, a short rubber tube, and a needle. The needle shaft is enclosed in a glass cover, and the hub contains a filter. The ampule contains the medication plus 2 cc. of helium gas under a pressure of 2 atmospheres. . . . The neck and tip of the ampule is contained in one end of the rubber tube; the hub of the needle is in the other end. . . . The glass needle-cover is removed just before the medication is to be given. The needle is inserted under the skin or into the muscle as usual. The tubing is pinched and released to be sure that blood does not return from the site. The tube is then bent to break the ampule-tip, with the bottom of the ampule held upward. (This is called "activating" the ampin). The gas forces the fluid into the injection site. . . . Ampins may be used for emergency or routinely. A study of efficiency showed a marked saving of time, both for the nurses and physicians. They are most helpful in the operating room or for acute needs. . . . The hazards of a gas embolism are very scanty, even if precautions are not observed. The local effects of injection are rarely notable. The amount of glass injected is scanty and detectable by analysis, but is less than that when a syringe-needle technique is used. . . . As in all new procedures, the proof of the pudding will be found when more people eat it.

Two notes concerning ANTI-HISTAMINES.—
An asthmatic who becomes refractory or 'fast' to epinephrine may again respond after the use of an A H drug. . . . A patient with hay fever may develop asthma after the use of A H drug. . .

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ARIZONA STATE HOSPITAL

A Medical Survey of Progress and Deficiencies*

By

ERNEST A. BORN, M.D. (Prescott)
LINDSAY E. BEATON, M.D. (Tucson)

R. E. H. DUISBERG, M.D. (Phoenix)
JOHN R. GREEN, M.D. (Phoenix)

The following information was obtained following complete investigations of the Arizona State Hospital from March 7-14, 1951, and compared with the thorough survey made by Dr. Grover A. Kempf in 1938 and the next and most recent study made by Riley H. Guthrie, M.D., Chief, Hospital Services Section, National Institute of Mental Health, just one year ago (March 13-19, 1950.)

1. *Definite progress* is obvious in spite of the increased overcrowding of patients due to the growing population of the State of Arizona, and deficiencies of staff and facilities due to inadequate budgetary appropriations to compensate for the increased needs. This reflects well upon the administration of the Board of Control and the Hospital Superintendent.

1. More staff physicians, nurses, psychiatric social workers, occupational therapists, clinical psychologists and specialized consultants have been working at the Arizona State Hospital during the past year than at any time in its history. This is a major factor in the development of a more effective treatment program. Deficiencies are still present, the major obstacle being a financial inadequacy.

a. The number of full-time *physicians*, apart from the Superintendent, has varied widely since 1941. In 1941 there were 3 doctors; in 1947 there were 5; in 1950, 9; and at the time of this survey there were 10 physicians.

b. A *neuropsychologist* assumed his duties as Director of the Laboratory of Neuropathology and Clinical Medicine in October 1950. This department is one of the few in existence in state mental institutions in the United States, and promises to be a stimulating influence. Autopsies are now being done at the Arizona State Hospital.

c. The number of *graduate nurses* has been increased from 11, in 1949, to an all-time high of 22 at the present time. During the past year Miss Alva Aber, R.N., has assumed duties as Director of Nursing. She holds a Master's degree in Nursing Education from Columbia Uni-

versity and is in the process of a complete reorganization of nursing services and has made arrangements to teach student nurse affiliates from other nursing schools. This program should prove to be one of the most stimulating features of the entire treatment schedule.

d. A full-time *Clinical Psychologist*, who holds a Master's degree in Psychology, and who is working on a thesis for his doctorate, assumed his duties during the past year. He has a staff of 6 *senior psychology students* from Arizona State College who are gaining experience in interviewing and testing on patients under his supervision.

e. *Three full-time social workers* are now employed, in comparison to one until this past year. One of these workers spends the majority of her time visiting patients and families extramurally.

f. *Two occupational therapists* are now directing the work of psychiatric patients in one unit, and of neurologic patients in another unit. A limited program of physical education and training is carried out by the assistant occupational therapist. No such assistant has been employed in the past.

g. To facilitate active treatment, more *consultants* have been called in from Phoenix during the past two years than at any time in the history of the hospital.

2. Emphasis has been increased on treatment and research rather than on custodial measures.

a. The *Neuro-Surgical Unit*, comprised of qualified Phoenix specialists, under the direction of one of us (JRG), with administrative offices in the Hospital Building, carries out diagnostic studies, upon the request of the Hospital staff, to determine the presence or absence of organic diseases of the nervous system. These studies include physical, neurologic, psychiatric, spinal fluid, x-ray (including pneumo-encephalography, ventriculography, and arteriography,) and electro-encephalographic examination. Other consultants are requested as indicated. Management is recommended in out-patients and voluntary admissions are cared for. Psychosurgery and other neurosurgery, including the surgical

*Subcommittee on Mental Health, Arizona State Medical Association.

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treatment of focal epilepsy, is now available under well controlled circumstances.

This Unit sponsors a monthly clinicopathologic conference on the first Wednesday of the month, which supplements the daily staff conferences of the Hospital staff.

During the past year this Unit has received national recognition for original work done in the field of Psychomotor epilepsy:

- (1) March 1950—Symposium on Psychomotor Epilepsy, at a joint meeting of the American Academy of Neurology and International League Against Epilepsy, Cincinnati, Ohio.
- (2) June 1950—Symposium on Clinical and Electrical Aspects of Temporal Lobe Disorders, at the American Electroencephalographic Society, Atlantic City, N. J.
- (3) December 1950—Electrocorticography in Psychomotor Epilepsy, at the Western Society of EEG, Reno, Nevada.
- (4) An invitation has been extended, expenses paid, to take part in the Western Institute on Epilepsy, in June 1951, Salt Lake City, Utah.

Two scientific publications have been accepted by the publishers and are now in press.

- (1) Focal Epilepsy of Psychomotor Type—Journal of Neurosurgery.
- (2) Electrocorticography in Psychomotor Epilepsy—Electroencephalography and Clinical Neurophysiology.

Both publications are by Green, John R., Duisberg, R. E. H., and McGrath, W. B.

b. *Psychiatric treatment* facilities have expanded during the past year. One year ago, standard electroshock convulsive treatment, hydrotherapy and sedation were the principal therapies. An *insulin coma* department under competent psychiatric and nursing supervision is now in operation for the first time since it was curtailed by war shortages. Two new *Reiter stimulators* of the latest type have been added this year for convulsive and subconvulsive treatments. *Sodium pentothal narco-synthesis* interviews have been increased for diagnostic and therapeutic purposes.

Wards for the care of syphilis, including treatment with malaria, tuberculosis and children with various types of cerebral palsy have been reorganized during the past year and are under much better control than in the past, in spite of limited physical facilities.

Voluntary and ancillary workers have been solicited during the past year. Gray Ladies and the Unitarian Church group are being organized to actively aid the hospital with volunteer work, under the direction of Dr. Robert Lentz, the Clinical Director.

A *limited out-patient service* has been established during the past year, both by the Hospital Staff and by the Neuro-Surgical Unit. All hospital and consultant facilities are available, but the limitations are obvious. The fact that there has been an increasing number of *voluntary admissions* to the Arizona State Hospital during the past several years is an indication of the change in emphasis from custodial to treatment facilities. A new high of 19 voluntary admissions was reached during February 1951, with an average of 15 per month during 1950.

3. The Florence Branch, opened several years ago, during the administration of Drs. John A. Larson and Jeremiah Metzger, has been considered unsuitable and uneconomic. The Legislature, backed by the Guthrie report of 1950, urged the evacuation of this Branch as soon as possible. This was carried out during 1950. It centralized the operation of the state mental institution, but it intensifies the need for increased facilities. This increases the hospital population by 350 patients.

A new receiving building is now under construction. This will eliminate the need of using the hospital building for admission purposes and will provide a segregated area for observation of voluntary and committed patients, a sorely needed facility. It is expected that this construction will be complete by the Fall of 1951. It adds only 75 beds.

A new laundry and five new cottages for physicians were completed during 1950.

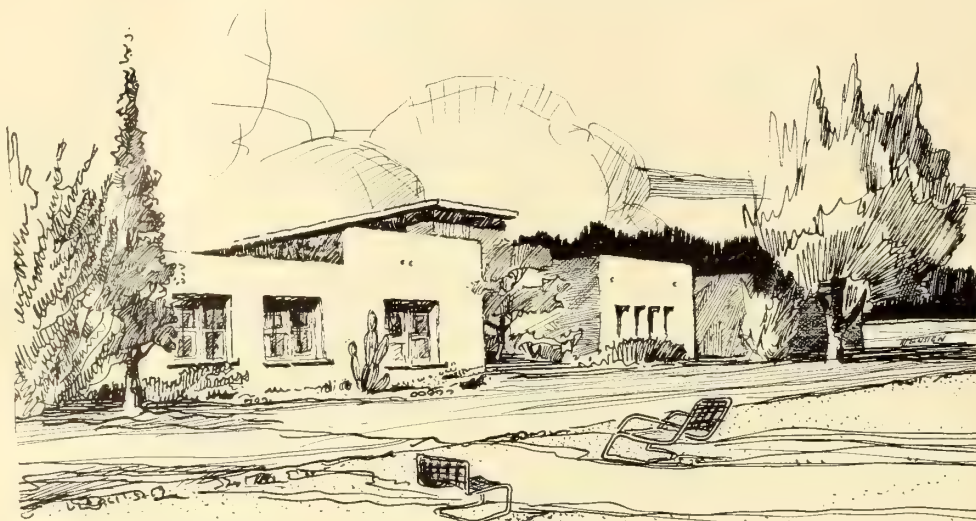
4. Progressive legislation passed this year for the benefit of the State Hospital includes: (1) A new commitment law, and (2) waiving of basic science requirements for State Hospital physicians.

It is obvious, therefore, that the principal gains made during the past year have been from the standpoint of administration, personnel and treatment, without appreciable changes in the physical plant.

II. *Existing deficiencies* are also obvious in spite of the efforts of the Hospital Administration. These deficits are felt to be due largely to public apathy which in turn is secondary to

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lack of mental health education and demand for adequate care for the mentally ill.

We hope that this report will give support to the Hospital management and offer constructive criticism to the end of obtaining a model mental institution for the state of Arizona.

The shortcomings are in two major categories:

1. Building facilities
2. Personnel

A beautiful hospital building offers nothing without adequate personnel, who create the spirit of the hospital; and, in turn, overcrowded, dismal, inadequate surroundings discourage the best of personnel.

1. *Building facilities* are dangerously inadequate. The rated capacity of the Arizona State Hospital is 919 beds. At this time there are 1592 patients occupying this space. The additional facilities created by the opening of the receiving wards (75 beds) and by the transfer of 50 children to the Arizona Children's Colony when it opens this next fall, will still leave a present need for 548 beds. This, of course, provides only for the existing problem and does not take into consideration the increasing numbers of people who will need such care.

Many states provide for 5 mental beds per 1,000 civilian population. On this basis Arizona would need 3,685 beds under ideal circumstances. Certainly definite plans should be made to increase the existing facilities by 500 beds during the next year, and another 1,000 beds during the next 5 year period.

A detailed 5 year building program has been prepared by the present administration to accomplish the needs and to meet the requirements for approval by the American Psychiatric Association. This has been submitted to the Interim Committee of the Legislature, in 1950. It has been reviewed, in detail, by this Committee, and is commended to the people of Arizona for adoption. (A copy of this program is attached.)

2. *Personnel*: This Committee commends the Board of Control and the Hospital Administration upon their accomplishments and has confidence that the correct reorganization of the State Department of Health, Welfare and Correction will be able to expand and to complete the objectives to establish a model mental institution.

The tremendous turnover of personnel at the Arizona State Hospital during its history is dis-

couraging to any type of treatment program. It is felt that the reasons for this turnover are: (1) Political, (2) poor surroundings and facilities, (3) lack of security, (4) lack of incentive to make a career of institution work, and, in some cases (5) poor selection of personnel. Fortunately, the first consideration is no longer of importance. The remainder of the factors listed are still present, to varying degrees.

a. A *state civil service or merit system* should be established which would prepare specifications and duties in all categories of positions, provide for promotions and retirement, and encourage employees to make the State service their career.

b. A *skilled personnel officer* should be employed full time by the Arizona State Hospital. He or she would be of invaluable help in the recruitment and selection of personnel, settling grievances, maintaining discipline, training programs, and public relations in general; under the overall direction of the Superintendent.

c. The position of *Assistant Superintendent* should be filled as soon as a qualified man is available.

d. More well qualified physicians are necessary to carry on the required amount of work. According to the American Psychiatric Association standards, one physician is essential for 200 resident patients, and one for each 100 admissions per year. In order to fulfill these requirements, the Arizona State Hospital should have 15 physicians, in addition to the Superintendent. *Five more qualified physicians are needed* in addition to the 10 now on duty, assuming that all ten of these doctors are actively engaged in the management of patients.

e. A committee rotated among various members of the Staff should be established to carry on the business of the Staff meeting each morning, thereby releasing the majority of the medical staff to ward duties. An increased staff is essential to the efficient operation of the Staff business and ward operations simultaneously. Under existing circumstances, it is apparently the ward work that suffers.

f. *More graduate nurses are also needed.* 25% of the nursing personnel should consist of graduate nurses. This would mean 54 graduate nurses, instead of the all time high, at present, of 22.

g. With accomplishment of needed increase in medical and nursing personnel it is recommend-

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ed that *proportionate expansion of ancillary services* should follow.

h. A modernization of the handling of *medical records* is indicated, in order to conform to the standards of the American College of Surgeons.

i. *Training programs* for student nurses, attendants, technicians, and college students in various departments should be intensified.

j. *Library facilities* for physicians, nurses, attendants, and also for patients should be established.

III. Summary of Recommendations.

1. Adoption and completion of the 5 year building program which was submitted in 1950 by the Hospital Administration to the Interim Committee of the Legislature.

2. Formulation of a State Civil Service and merit system for employees.

3. Employment of a trained personnel officer by the Arizona State Hospital.

4. Appointment of a qualified Assistant Superintendent.

5. Employment of qualified and active physicians to meet the minimum quota of 15, in addition to the Superintendent, set by the American

Psychiatric Association.

6. Employment of sufficient registered nurses to meet the American Psychiatric Association standard of 25% of all nursing personnel, a minimum quota of 54 registered nurses.

7. Increase of ancillary services proportionate to increased medical and nursing services.

8. Definite training programs for all personnel.

9. Improved medical record and library facilities.

IV. *Conclusions:* We commend the Hospital Administration, and particularly Dr. Bruce D. Hart, Superintendent, on the progress that has been made during the past year, despite adverse circumstances. Existing deficiencies are emphasized and constructive criticism is offered. We consider it to be the duty of each citizen of the State of Arizona to insist upon adequate facilities for the care of the mentally ill, both for humane and economic reasons. This Committee pledges its support of this program to the Department of Health, Welfare and Correction, and is confident that its successful completion is attainable in the near future.

ANNUAL REPORT, INDUSTRIAL RELATIONS COMMITTEE

This committee began its duties on June 1, 1950. It consists of five members, four of whom were carried over from the previous year and one new member. Meetings were held once a month in Phoenix, some of them with the Industrial Commission and some of them by the committee alone, considering matters brought to its attention by the Commission.

Following the meeting of this group, functioning as the Industrial Relations Committee, it was picked up by the Industrial Commission as the Medical Advisory Board. In this capacity it held one meeting which lasted one or two days. Industrial injury cases were sent to this Board by the Industrial Commission. Examinations were made and recommendations as to disposition given to the Commission.

When acting as the Industrial Relations Committee, we were asked to review many files in order to determine fair fees for doctors' services. We found that the Fee Schedule of the Industrial Commission did not include all of the procedures for which doctors billed the Commission. In order to arrive at fair and equitable

charges, it was sometimes necessary to consult the Blue Shield fee schedule as well as schedules from California, New York and Illinois. We recommended to the Commission that their Fee Schedule be brought up to date with fee revisions where indicated. We also advised that the new Fee Schedule be much more complete with the various procedures coded. A new schedule will entail a great deal of work but should be ready in the near future.

During the preceding year we recommended that injury cases who did not improve as expected should have neuropsychiatric evaluation. This program bogged down for several reasons and routine referral of such cases by the Commission is not being made. We would like to bring to the attention of all physicians doing Industrial work, the suggestion that neuropsychiatric consultation be asked of the Commission when recovery is not prompt. This applies particularly to back cases.

On March 13, 1951, some of the members of the Industrial Relations Committee were able to meet in Phoenix with Dr. J. F. McCahan,

assistant secretary to the Council on Industrial Health of the American Medical Association. Dr. McCahan stopped in Phoenix while making a field trip through the Southwest. He urges that doctors doing industrial work make themselves familiar with the plants for which they render medical services. He felt that all concerned would benefit by the doctors familiarity with both industrial and health hazards. He also felt that anything we could do as doctors working with management to help improve the health of employees and their families, would help prevent the Federal Government from moving in on this particular phase of medicine.

Respectfully submitted,

Carl H. Gans, M.D., Chairman

Charles W. Sult, Jr., M.D.

Ronald S. Haines, M.D.

Joseph P. McNally, M. D.

John R. Schwartzman, M.D.

***REPORT OF LEGISLATION COMMITTEE CHAIRMAN**

The Legislation Committee of our Association sponsored three bills for introduction in the First Session of the Twentieth Legislature of this State. These were:

1. H.B. 83, An Act creating an Anatomy Board; providing for the disposal of dead human bodies for scientific purposes, etc.

2. H.B. 84, An Act relating to Public Health and providing for the vivisection of animals.

3. H.B. 85, An Act relating to the Basic Sciences and the Practice of Medicine, providing exemptions, etc.

For the first time this year Council provided funds in the Budget of Appropriations for use by this Committee for the purpose of research in the preparation of our bills and the employment of personnel in the preparation and promotion of our program. Mr. Edward Jacobson, prominent Phoenix attorney, prepared these measures in proper legal terminology; and served very effectively in liaison between our Central Office and the members of the Legislature.

Two of our bills, one relating to the creation of an Anatomy Board and the other to the Basic Sciences and the Practice of Medicine, successfully passed the House and Senate, while that relating to vivisection of animals passed the House, only to be reposed at the close of the Session in one of the Senate committees. There was an avalanche of opposition from interests

both inside and outside the State to this measure in the Senate and to the Governor, and no amount of pressure or effort could extricate the bill from the Senate committee.

Representatives of our Committee, the Council, some members of the Maricopa County Legislation Committee, and the Executive Secretary appeared in open hearing for over three hours in the afternoon of February 21, 1951, before the House of Representatives in protest of the proposed amendments to the Naturopathic Practice Act wherein members of this group of practitioners wished to expand their practice to permit of the prescription of substances of plant, animal or mineral origin as are naturally found in and required by the human body, herbs, cell salts, plants, roots, barks, mineral and vegetable oils, antiseptic, germicidal, and bacteriostatic agents, non-habit forming anodynes and vitamins, and to do simple minor surgery and natural obstetrics. Mr. Jacobson represented the Association as its spokesman and performed his duty in a dignified and effective manner. Our efforts blocked enactment of this piece of legislation.

The Council of our Association acted upon the bill sponsored by a group of legislators serving as an Interim Committee of both Houses of the Legislature who, with the help of experts in the field of economy in state government, presented the reorganization bill relating to Public Health, Welfare and Correction, H.B. 46. With full knowledge of an expected unprecedented approval of this bill on the part of the members of both Houses and the Governor, no effort was expended by this Committee to amend the bill, except to send copies of the following resolution to key Committee Chairmen in both Houses:

Whereas, The provisions of H.B. 46, State of Arizona, Twentieth Legislature, Regular Session, have been read and discussed at a meeting of the Council of the Arizona Medical Association on January 21, 1951, and

Whereas, It is evident that under the provisions of said H.B. 46, the Director of Public Health would become a staff member of the Commissioner of the Department of Public Health, Welfare and Correction, a political appointee, and

Whereas, The administration of public health measures should always be free from many possibility of political pressure, now therefore

*Report of Legislative Committee condensed.

Be it Resolver, That the Council of the Arizona Medical Association hereby registers its disapproval of proposed H.B. 46 as it relates to the Department of Public Health, and

Be it Further Resolved, That the Department of Public Health of the State of Arizona be not included in H.B. 46 but that it continue to be a separate Department of the State of Arizona, and

Be it Further Resolved, That the action of this Council be made known to the Committees of Public Health of both Houses of the Twentieth Legislature of the State of Arizona, as well as to the public of the State of Arizona through the press, and

Be it Further Resolved, That in the opinion of the Council of the Arizona (State) Medical Association the above suggested revisions are necessary in the interest of the protection of the health of every citizen of the State of Arizona.

Through action of approval by the Council, your Legislation Committee gave active support through personal interviews and letters to the following measures which were introduced:

1. H.B. 53, An Act relating to Nursing and to provide for examination, licensure and regulation of persons who practice nursing.
2. Sub. H.B. 192, creating an Arizona Youth Authority.
3. S.B. 88, creating a Board of Physical Therapy Examiners and prescribing powers and duties.
4. Approved expansion of the activities of the State Department of Public Health as pertains to the State Laboratory.
5. H.B. 93, relating to Mentally Ill Persons, providing for procedure for their apprehension, detention, and committment to the State Hospital.

The Committee wishes to express its appreciation to Mr. Jacobson, members of the Council, members of the Maricopa County Legislation Committee, the Executive Secretary, and others of our Association who gave of their time in the interest of sound health legislation.

Jesse D. Hamer, M.D.
Chairman

REPORT OF COMMITTEE ON MEDICAL DEFENSE

Annual Meeting 1951—Council, April 29, 1951;
House April 29, 1951.

Committee members: O. E. Utzinger, E. A. Born, F. W. Knight.

1. Since the annual meeting of May 1950, \$817.20 has been expended on two cases of alleged malpractice filed against Society members.

2. There are at the present time of record, ten cases in various stages of litigation.

3. The Medical Defense Fund, now the "Reserve Fund", is at present \$39,591.20, \$36,000.00 in bonds, \$3,591.20 in cash. This is a gain of \$156.58.

4. At the 1950 Annual Meeting among other items the following was approved by the House: "that in the case of suits filed for alleged malpractice occurring subsequent to December 31, 1949, legal counsel be furnished by the Medical Defense Committee if deemed necessary, on the request of the defendant physician and his counsel, *with the approval of the Medical Defense Committee*, such cost involving current cases of alleged malpractice to be financed from the interest derived from the bonds."

Your committee would like very much to have clarified by the House the above quoted portion of the adopted resolution. For several years the members of the Medical Defense Committee have routinely approved the expenditures on all cases that have been sent to us by the central office. We have never investigated a single case, nor are the three present members of your committee, all living in outlying and sparsely populated counties, in a position to properly judge which cases should or should not be "deemed necessary" for defense. It would seem to be necessary that either all cases be approved regardless of merit or else that a proper court of inquiry be set up to investigate each case.

5. The Medical Defense Committee recommends: a. That the one dollar yearly deduction per member for medical defense be continued: b. That the Medical Defense Fund (Reserve Fund) be for medical defense solely, the purpose for which it was originally intended.

O. E. Utzinger, M.D.
Chairman

ANNUAL REPORT OF THE PROFESSIONAL BOARD ARIZONA MEDICAL ASSOCIATION 1950-1951

Meetings of the Professional Board were held in Tucson on September 10, 1950 and in Phoenix on February 25, 1951. The membership

of the Board attended in a satisfactory manner.

The Seminar program this year was limited to a Fall series on "Defense Against Atomic Warfare." This program was presented not only in Maricopa and Pima, but also in the outlying counties. Expenses for this amounted to \$932.11 for separate meetings from September 11, 1950 thru October 22nd, 1950. It is of interest to note that this was one of the very first of the so-called defense measures undertaken by any group in the state. It is suggested by the Seminar Committee and the Board that next year's program continue the custom of having seminars conducted by members of the Colorado Medical School Faculty as in previous years.

The subcommittee on Maternal and Infant Welfare is gathering together a fair-sized number of death certificates of mothers for the year 1950. The survey of these is felt to be a potential source of information, and questionable diagnoses will be further investigated by forms mailed to the attending physician.

The Hard of Hearing program continues to function with increased efficiency. School surveys are continuing in Maricopa, Pinal, Yuma and Gila counties. Courses for speech defects are being planned at the University of Arizona and State College for the coming summer. It seems manifest that the enthusiasm for this program, engendered by the work of Mrs. Lydia Newton and the Chairman of our committee, Dr. Joseph M. Kinkade, has launched a very wide-spread and very successful program in the state.

The subcommittee on Tuberculosis made a survey of all physicians in the State of Arizona who had pneumothorax equipment in their offices and would be willing to care for ambulant cases discharged from the sanatorium. A very excellent response was received and the information turned over to the medical director of the State Tuberculosis Sanatorium. The committee has drawn up recommendations in regard to the tuberculosis situation in Pima County, and has been active in all organizations interested in tuberculosis treatment and control.

The subcommittee on Mental Health has been extremely active and has been assigned a difficult task. There has been a very close observation and a very active cooperation by the members of this committee with the Arizona State Hospital. Improvements in many lines have become apparent as a result, or certainly

concomitantly. The committee has met with the superintendent of the State Hospital to investigate charges made by a recently discharged employee, a physician who gave the hospital much adverse publicity thru the medium of a front page story in the Phoenix papers. The investigation revealed that this publicity was uncalled-for and that the charges were unfounded. The committee continues its endeavors to improve the commitment procedure in the State of Arizona, and at last has had a bill passed establishing more up-to-date methods. This sub-committee was presented the problem raised by the Arizona Psychological Association which requested the state societies reaction to the problem of licensure of or registration of psychologists within the State of Arizona.

The subcommittee on Cancer has continued to cooperate with the American Cancer Society, not only thru its educational program, but also thru its operation of cancer clinics and detection centers.

The Venereal Disease Committee was extremely active in sponsoring educational programs thru all media, including radio, newspaper, and talks before civic and lay groups.

Many miscellaneous problems have been presented to the Professional Board for clarification, study and recommendation. The committee has cooperated with the Public Health Department, in the person of Dr. Ward, and has lent its support to his urgent request for better reporting of communicable diseases. Communications have been received from diabetic control organizations, industrial hygiene and health organizations and from many other national groups, as well as from state organizations requesting information and cooperation. These matters have been given consideration and appropriate action was taken. The Professional Board has recommended to the Council action with respect to the education of Arizona medical students in out-of-state universities.

The Board respectfully recommends:

- I. That seminars be continued in the outlying counties with adequate budgetary consideration being given for such seminars.
- II. That this board be increased by one more subcommittee to be known as General Medical Subcommittee which might act on the problems of geriatrics, industrial health, diabetes, and other such specific national health movements more effectively.

- III. That the council recommend to the State Legislature some program for the support of Arizona medical students in out-of-state schools by subsidy to those schools, much as is done in other states without medical institutions of learning.
- IV. That there should be an active campaign of publicity to counteract the inept anti-medical antivivisection advertising which has appeared in the daily press and circulars.

Respectfully submitted,
Arthur J. Present, M.D., Chairman
Professional Board
Arizona Medical Association

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INDUSTRIAL HEALTH CONFERENCE

**ACTH, CORTISONE COMBATS
NEW PULMONARY DISEASE**

Successful application of the new drugs, ACTH and cortisone, in retarding the deadly effects of a new pulmonary chest disease, chronic berylliosis, was described today before the American Association of Industrial Physicians and Surgeons by Dr. H. E. Tebrock of Sylvania Electric Products, Inc.

Citing chronic berylliosis as a disease resistant to most forms of therapy, Dr. Tebrock said that nearly all types of treatment have been tried in the past with improvement rarely noted. In one area, of 86 cases treated, 24 died, 31 were totally incapacitated, 17 could continue work only on a limited basis, and there was no assurance that the remaining cases were permanently cured.

The disease, which attacks the lungs and occasionally other organs, is believed to result from small amounts of beryllium, which are present in some industrial chemical compounds, entering the body and being released through the tissues in minute amounts.

When ACTH was first tried, the patients showed more improvement than from any previous treatments. After several cases were treated with ACTH, it was decided to try cortisone to offset undesirable side effects from the treatment. This proved equally satisfactory, Dr. Tebrock said.

"We hope to retard or prevent the progression of the disease to a more fibrotic state by the use of the drugs," he declared. "We are making no claims, but we feel that the apparent symptoma-

tic improvement, in the sense of well-being induced by this form of treatment, has warranted its use so far."

Dr. Tebrock cautioned, however, that ill effects might result from the continued use of the drugs. He said that the possibility of adrenal and pituitary atrophy must be considered.

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**700 PHYSICIANS OPEN FIVE DAY SESSION
ON INDUSTRIAL MEDICINE**

Nearly 700 of the medical men responsible for keeping American workers safe and healthy in their jobs convened here today to discuss their work and its relation to the nation's defense effort.

Attending the five-day conference of the American Association of Industrial Physicians and Surgeons are health leaders employed by business and industry to guard the physical welfare of employees. The association's meeting is being held in conjunction with the 1951 Industrial Health Conference attended by 2000 physicians, dentists, nurses and hygienists.

A major subject for discussion will be the role of industrial medicine in civil defense. A two-hour program on this subject will include reports from Brig. Gen. Otis B. Schreuder, USAF, and Commander E. Richard King, USN.

The convening medical men will also deal extensively with the medical and economic problems of retirement of employees.

A total of 16 papers dealing with civil defense and industrial illnesses and accidents will be presented at conference sessions. Additional discussions of specific problems will be held at special sectional meetings.

The association will participate in a joint meeting of all the industrial health organizations on April 25. The entire session will be devoted to "New Developments in Industrial Health" and "Teamwork in Control of Occupational Diseases."

The latter program represents the first comprehensive report on the cancer control program developed by Standard Oil Company (New Jersey) for the protection of its employees and the employees of its affiliated companies. Its results will be outlined by four physicians and one industrial hygienist engaged in the program.

PERSONAL NOTES

Drs. Paul Armour, Donald Carlson, Clyde Barker, Jr., Lucille Dagres, and Roland Hussong, of Phoenix, attended the American Academy of General Practice, Scientific Assembly, San Francisco, California, March 19-22, 1951.

Paul M. Roca, Phoenix attorney, addressed the March 19th St. Monica's Hospital Staff Meeting on "Medico-Legal Problems."

Dr. Paul Case, Phoenix, reported a "Case of Sympathetic Ophthalmia Treated with ACTH", at the March 26th Good Samaritan Hospital Staff Meeting.

Dr. C. Wm. Weisser, of Pittsburgh, Pennsylvania, and Dr. Howard Morrison, Omaha, Nebraska, addressed the March 26th Good Samaritan Staff Meeting on "Specificity in Ophthalmic Therapy."

Two cases were presented of "Periarthritis Nodosa and Diffuse Collagen Disease" by Dr. Albert Eckstein, Phoenix, at the Good Samaritan Hospital Staff Meeting, March 26th.

Dr. James M. Ovens, Phoenix, has moved his office to the Professional Building.

Dr. E. E. Reddick, Phoenix, has resigned as Director of Local Health Administrator, with the Arizona State Department of Health, to become Co-ordinator of Local Health Services in Kentucky. He has moved to Louisville, Ky.

Dr. Clarence G. Salisbury, Phoenix, will become the first Commissioner of Health, Welfare and Correction. His department is to be activated July 1st. He has been Chief of the Bureau of Preventive Medical Services in the State Health Department.

Dr. William G. Furth, Phoenix, has volunteered for duty and left his practice in Phoenix to join the U. S. Air Force Medical Department. His basic training will be taken at Randolph Field, Texas.

Dr. Wallace Meyer, Phoenix, spoke before the April 9th St. Joseph's Hospital Staff Meeting on "Lymphoblastoma of Anus and Rectum."

The April 16th Staff Meeting at the newly named "Memorial Hospital"—formerly St. Monica's, was filled with "A Case of Abscess of the Epiglottis"—presented by Drs. Jerome Kaye and John Kruglick, Phoenix. This was discussed by Dr. Jack Brooks, Phoenix. The meeting was concluded by a presentation of "Diagnosis and

Treatment of Hip Disease in Children" by Dr. Raye Fife, Phoenix.

Dr. Burnett, of Southwestern Medical School in Texas, spoke before the Osler Club in Phoenix, April 19th on "Acute Urinary Suppression and its Treatment."

Dr. Raymond Huger, Phoenix, spoke on "Meckels' Diverticulum", before the St. Joseph's Hospital Staff Meeting May 14, 1951.

Dr. Thomas Bate, Phoenix, was elected President-elect of the Arizona Medical Association at its 60th annual meeting in Tucson, Arizona, April 29th-May 2, 1951.

Dr. Kent Thayer, Phoenix, was elected Councilman at Large.

Dr. M. J. Whitelaw, Phoenix, is presenting several papers in Atlantic City, New Jersey, June 1951. He is presenting an A.M.A. exhibit on "Cortisone and ACTH in Burns." Before the American Society for the Study of Sterility, he speaks on "Some Concepts in the Physiology of the Basal Body Temperature Pattern." Before the Association meeting for the Study of Internal Medicine, he is presenting "Observations on the Use of Oral Cortisone and ACTH in the Open Treatment of Burns", and "Clinical Observations on the use of ACTH in the Peripheral Bed." With Dr. Stahnke of Tempe, he is presenting "Effects of ACTH in Scorpion-Neuro Toxin."

Dr. Whitelaw wishes to point out here that his experiments with Dr. Stahnke indicate that the use of ACTH in rattlesnake and blackwidow spider bites is contra-indicated, in spite of the fact that Armour and Co. have literature published which recommends its usage. Rats are put into convulsions by ACTH following rattlesnake and blackwidow spider bites.

At the May 16th Staff Meeting of Memorial Hospital, Dr. H. L. Williams, Phoenix, spoke lengthily on "Common Anorectal Disorders." Dr. Thomas Read, Phoenix, presented a "Primary Carcinoma of the Lung Following Breast Carcinoma."

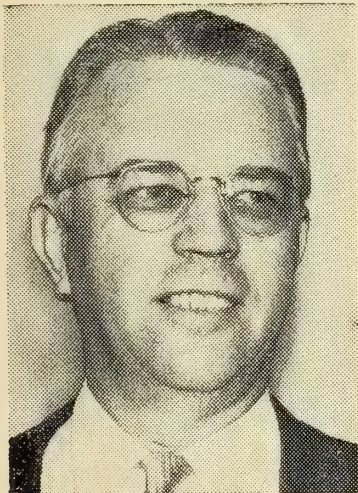
Dr. Marcy L. Sussman, Phoenix, spoke before the 69th annual session of the New Mexico Medical Society, Santa Fe, New Mexico May 4, 1951, on "Obscure Gastro-Intestinal Bleeding" and "Non-Tuberculous Disease of the Lungs."

Drs. D. W. Melick and C. T. Read, Phoenix attended the meeting in Atlantic City of the American Association for Thoracic Surgery on April 16th, 17th and 18th.

On April 19th Dr. Melick appeared before the

American Board of Thoracic Surgery in New York City to take the second and final part of the examination for certification by this Board. He has since been informed that he was successful in passing the examination.

Dr. George S. Enfield, Phoenix, recently has been certified as a Fellow of the American College of Anesthesiology.



EXECUTIVE SECRETARY F. G. MITTEN

Appointed to fill the newly created post of executive secretary to the Maricopa County Medical Society is Frederick G. Mitten, former New York publicist and advertising agency executive.

ARIZONA ASSOCIATION OF
PATHOLOGISTS & RADIOLOGISTS

At its meeting of April 29, 1951, the Arizona Association of Pathologists and Radiologists voted to disband to allow the organization of separate organizations for the radiologists and the pathologists. It was felt that the number of radiologists and pathologists had increased sufficiently to make this move advisable. The radiologists re-organized as The Arizona Radiological Society and elected the following officers: President—Dr. Maurice Richter, Phoenix, Arizona; Vice President—Dr. Herbert D. Welsh, Tucson, Arizona and Secretary-Treasurer, Dr. R. Lee Foster, Phoenix, Arizona. The pathologists organized the Arizona Society of Pathologists with the following officers: President—Dr. George O. Hartman, Tucson, Arizona; Vice President—Dr. O. O. Williams, Phoenix, Arizona and Secretary-Treasurer, Dr. Ralph H. Fuller of Tucson, Arizona.

R. Lee Foster, M.D., Secretary

WOMAN'S AUXILIARY

ANNUAL REPORT OF THE
WOMAN'S AUXILIARY
TO THE
ARIZONA MEDICAL ASSOCIATION

As President of the Woman's Auxiliary to the Arizona Medical Association, I wish to send greetings to the President, Mrs. Herold, and to all National officers, from the Auxiliary members in Arizona.

The following is a report of the 1950-1951 activities of the Auxiliary:

Organization: The current membership is 350, an increase of ten members over the preceding year. Organization is still confined to the four counties, Pima, Yavapai, Maricopa and Gila. There are 32 members at large.

Programs: The program chairman at all times urged the county groups to plan varied and interesting programs along the lines suggested by National, and also recommended the need to study legislative issues. Self-education on all phases of compulsory versus voluntary health insurance, which would lead to a more enlightened membership, was stressed, as well as the furthering of friendly relations between the Auxiliaries and other organizations.

Public Relations and Health: Public Relations and Health Chairmen and the Auxiliary President were privileged to meet with certain of the public relations committee of the State Association last summer for the purpose of planning a program wherein the Auxiliary could best help the Association in furthering public relations projects. After much discussion, two courses of action were agreed upon. First, to assist the Association with the endorsement drive started by it some months previously. Second, to urge each county auxiliary to do its utmost in shouldering civic responsibility in its own community, with special emphasis on health problems. Letters and literature were sent to numerous organizations with the suggestion that a study be made of the issue of compulsory versus voluntary health insurance, with the hope that understanding would bring a resolution in favor of medicine's stand. The controversial nature of the subject and, in some instances, by-laws prohibiting groups from acting officially on such questions, particularly

where there was a national affiliation, presented many difficulties. The following organizations did pass resolutions and these are filed in the Chicago office of the American Medical Association: Tucson Chamber of Commerce, Globe Parent-Teacher Association, Business and Professional Women's Clubs of Yuma, Bisbee, Kingman and Tucson.

We have done constructive work in presenting the problem of compulsory health insurance to the American Association of University Women and the Parent-Teacher Association groups on the local scene. Proper officers were contacted, kits especially prepared by Whitaker and Baxter were forwarded to these officers, and in response to a telephoned plea for help from the National Education office, local auxiliary members affiliated with A.A.U.W. sent telegrams to the Resolutions Committee of the A.A.U.W., at its biennial convention held the early part of April. We are most gratified to learn that the issue of compulsory health insurance has been placed on the national study agenda of A.A.U.W. for the first time. We feel that in our small way, we were helpful in the effort made to bring this to pass. We will continue to watch activities of this group and the Parent-Teacher Association, in the State and communities, and do everything possible to encourage action.

Philanthropic: The membership assisted both physically and financially in Red Cross, Community Chest, Cancer, Polio, Crippled Children and Tuberculosis drives. An entire room was completely furnished in the Gila County Hospital by the small auxiliary membership of 13 women. Yavapai, with a membership of 11 active and 12 associate members, has done a tremendous job in presenting the work of the Nurse's Loan Committee to the lay public, as well as donating generously to the above mentioned agencies, the Salvation Army and the purchasing of oxygen tents for the Community and County Hospitals in Prescott. Maricopa and Pima, the two larger counties, have participated in all of the drives above mentioned, as well as having donated generously to them. In addition, Maricopa Auxiliary furnished supplies and two volunteer workers each week to the Visiting Nurse Association and gave many hours to the County Chest X-ray campaign. Pima Auxiliary helped further the Adult Educational program of the American Cancer Society, to-

gether with the placing of sound film on the subject when and where requested.

Student Nurse Loan: This is our most ambitious public relations project. Applications are accepted from girls in the State who have the necessary grade and health qualifications. Contact is made through the high schools. This year 4 girls have been assisted. The fund is financed by auxiliary members and the members-at-large and will be self-sustaining in a five year period. This project has received state recognition from the nurse's associations, high school principals and lay organizations, and we believe it to be of inestimable public relations value to both the Auxiliary and the Arizona Medical Association.

Legislation: Auxiliary entered into an all-out campaign to see that doctors and their wives were registered so that there would be no slip-up at the time of local elections. When our 20th Legislature went into session, we were apprized of the bills in which our Association was interested, those it disapproved and those it sponsored. Copies of the bills were secured, a digest made and mimeographed and sent to all auxiliaries for distribution and discussion and also mailed to the members-at-large. National legislation was passed on to the county groups and the members urged to act individually when the occasion indicated.

Today's Health: Inasmuch as this is an authentic health magazine published by the American Medical Association, the Auxiliary considers its work in helping in the distribution, an opportunity to further health education. Subscriptions have been donated to schools and hospitals. We hope some day to encourage every doctor in the State to subscribe as it is excellent waiting room reading material. Our subscriptions increased by 75 this year. Yavapai Auxiliary was given National recognition in the contest with a listing in Group I—the first ten auxiliaries having the highest percentage per membership. We are also proud to mention that last year's Today's Health chairman, Mrs. George Enfield, received National recognition when an article written by her for the Arizona Medicine, was used in the Handbook for Today's Health printed this year.

Bulletin: One hundred forty Bulletin subscribers were purchased by members and members-at-large.

Historian: The year's activities have been

recorded in the State records, and the historian has submitted a complete State history as requested by the National Historian.

Publicity: Auxiliary articles were printed in Arizona Medicine each month, and special events were given fitting newspaper notices.

We are deeply grateful to the men of the State Association for their moral support and leadership as well as their financial support, for again this year we were given \$1000.00.

It was our honor and privilege to entertain the National President, Mrs. Herold, during our State meeting. The joy of her presence and the inspiration we received from her message, successfully completed a year of activity and accomplishments.

Respectfully submitted,
Mrs. Benjamin Herzberg, President
Woman's Auxiliary to the Arizona
Medical Association

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PROPOSED PROGRAM 1951-52

At the Chicago Conference of Presidents and Presidents-elect last October, the "Healthy Living" discussion, led by Mrs. William M. Gambrell of Texas, impressed me very much. After studying the complete kit of information on this Health Education Program, I turned it over to the next year's state chairmen of Public Relations and Health Education for study and consideration. They feel it would be an excellent program for both committees to undertake in Arizona in 1951-52.

Since our Organization Chairman has not been elected, her plans can not be incorporated in this report, but the auxiliary board hopes that next year at least one new county auxiliary will be organized and the numbers of members-at-large increased.

The Publicity Committee will continue the news column in *Arizona Medicine* with some variance in subject matter. If the trial news letter being sent out this spring to all doctors' wives in the state proves successful, it may be repeated next year.

The *Bulletin* and *Today's Health* chairmen will start making plans soon to increase the sale of these publications. We hope for a banner year.

Last May the Nurses' Loan Committee set up qualifications and policies for girls requesting financial aid during their nurses' training. All

high school principals received duplicate letters, applicants were interviewed and loans given to four girls. One girl received a maximum loan of \$300.00; three girls received partial scholarships totalling \$300.00. The committee felt it was wiser to send letters to the principals in February this year, so applicants are being interviewed now for the second year loans in order that actual voting on the girls can take place at the state convention.

The board feels that the work accomplished by this committee has been gratifying and from a public relations standpoint, it has no equal. The Woman's Auxiliary has gained respect; the state Nurses' Association has become familiar with the project and the girls benefited; school principals have sent letters of congratulation; hospitals throughout the country have been watching this national program of the Auxiliary. We hope to keep the ball rolling until such time as the program becomes self-sustaining.

Having personally attended the Annual Conference in Chicago last fall, I can testify that paying the expenses of the President-elect is money well spent. It gives her inspiration, understanding and new ideas to bring back to her state auxiliary. I am sure the new President elect will feel that she, too, is gaining much when she attends the conference next fall.

Before closing this brief summary of a full program, I wish to say that I realize the tremendous responsibility I have assumed but appreciate the confidence the Medical Auxiliary has shown in electing me to this position. And to the doctors I pledge my loyalty and that of the Auxiliary. We shall stand ready at all times to serve the Arizona Medical Society.

In closing, I wish to say that the board has authorized me to request of the Arizona Medical Society \$1,000.00 to aid in carrying out the program of the Woman's Auxiliary for 1951-52.

We hope it will be possible to have this program approved before the post board meeting, May 1st, so if the Health Education Program is to be undertaken, the Public Relations and Health Committees can make their intital contacts with the schools before their closing date in May and this summer start the ground work for next winter.

Thanking you for all considerations, I am
Respectfully,
(Mrs. Royal W.) Brownie Rudolph,
President-elect



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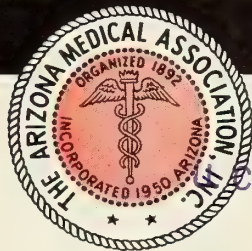
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VOL. 8, NO. 7



JULY, 1951

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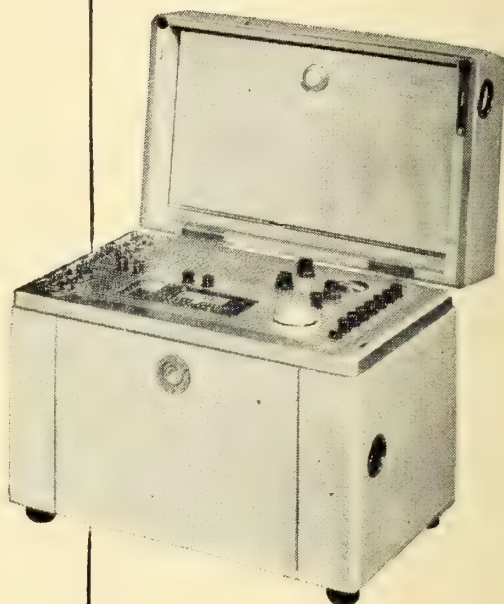
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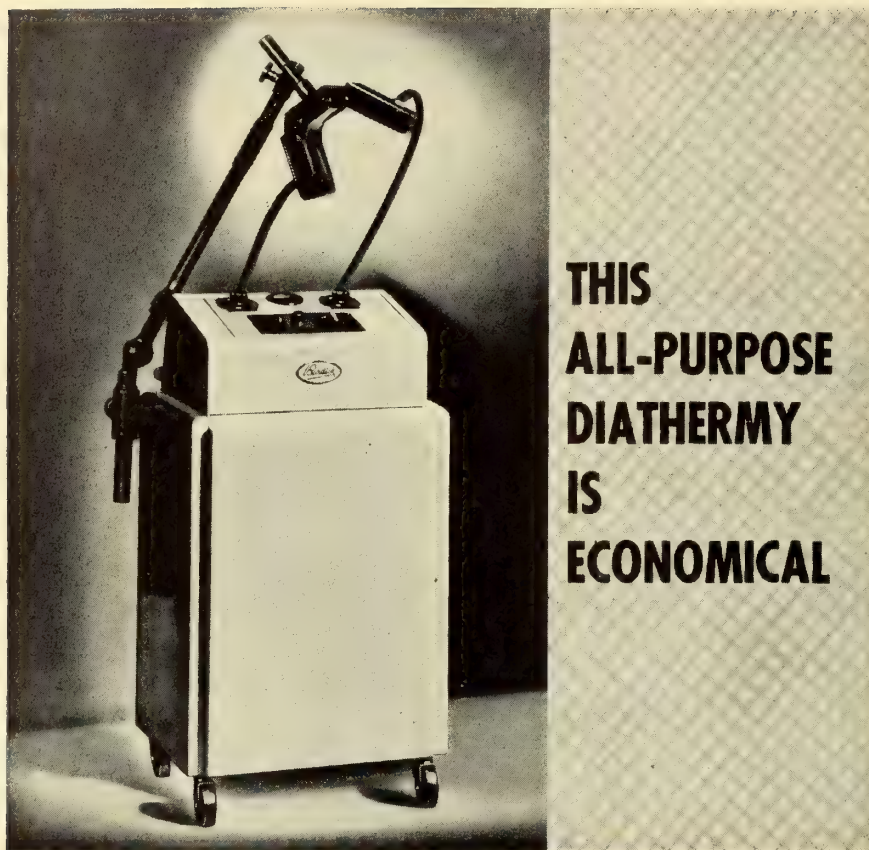
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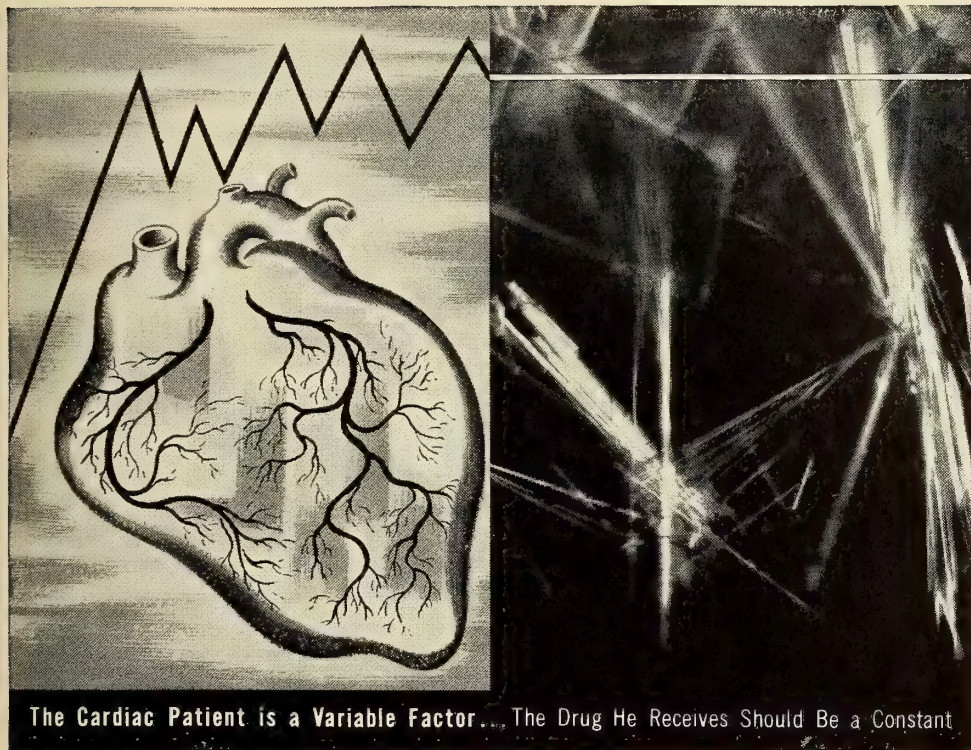
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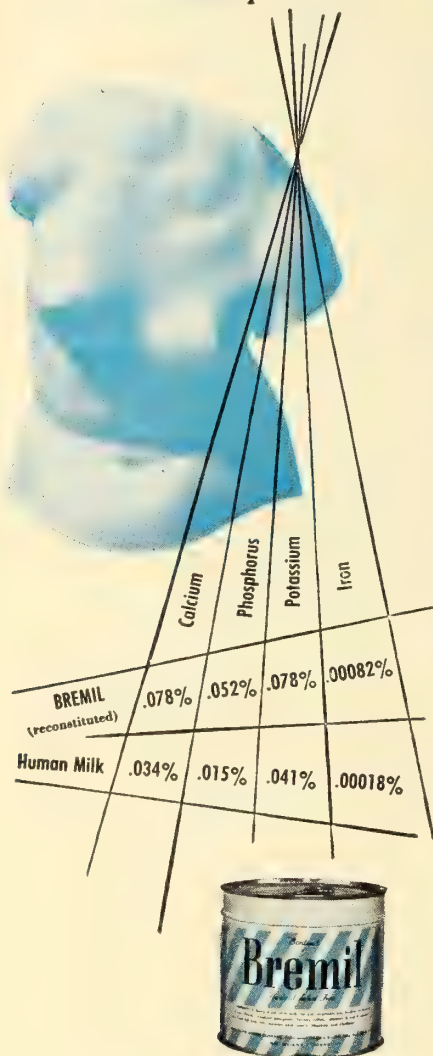
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1. Gardner, L. I.; MacLachlan, E. A.; Pick, W.; Terry, M. L., and Butler, A. M.: *Pediatrics* 5:228, 1950.

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4. Recommended Daily Dietary Allowances, Rev. 1948, Food & Nutrition Board, National Research Council.

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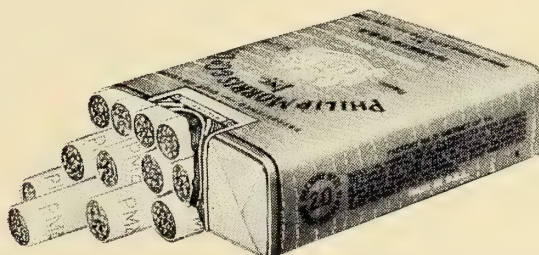
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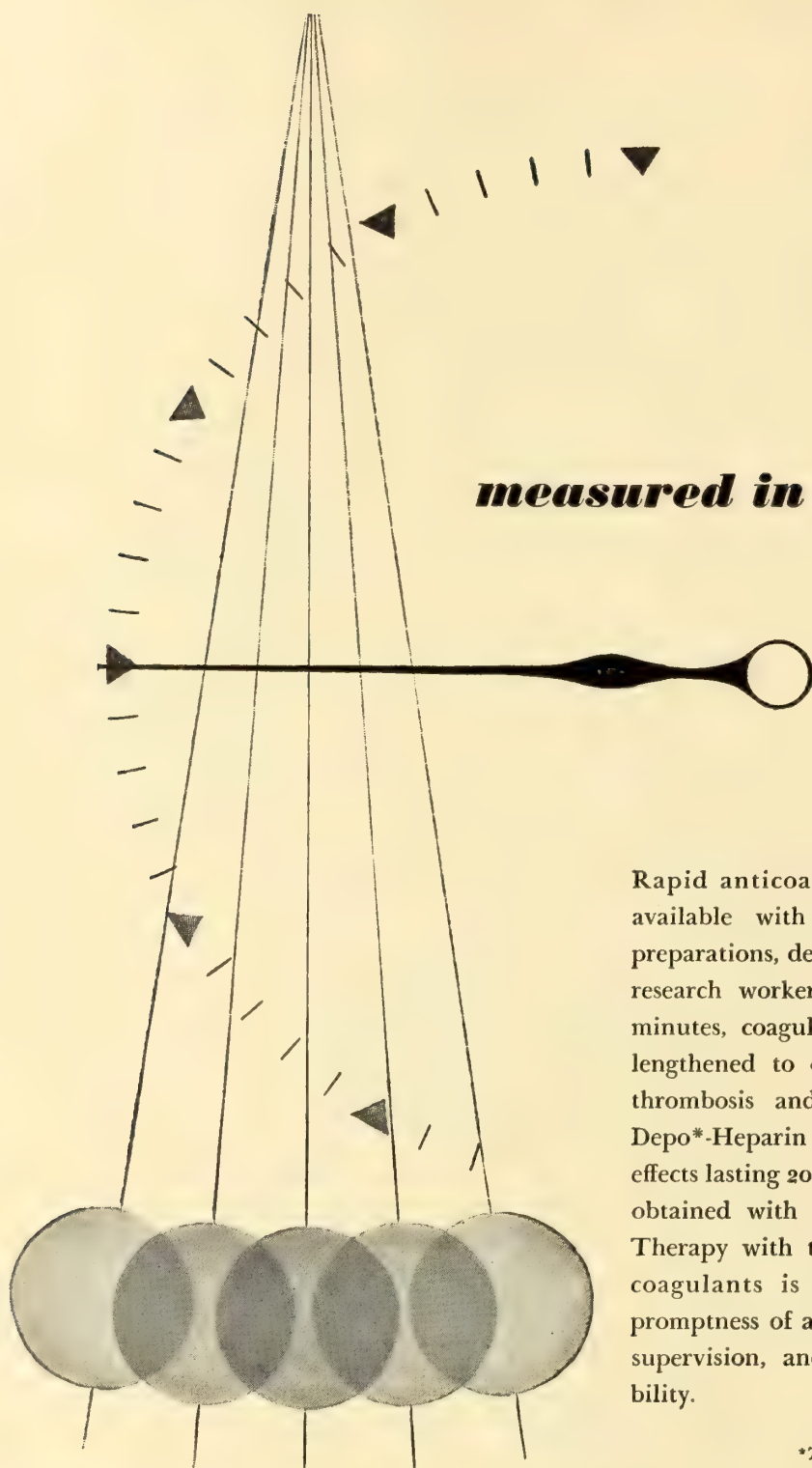
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References:

1. Burke, B. S. and Stuart, H. C.: J.A.M.A., 137:119, 1948.
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6. National Research Council: "Recommended Food and Nutrition Board, Daily Allowances for Specific Nutrients," Wash., D. C., 1948.
7. People's League of Health: J. Lancet, 2:10, 1942.

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REFERENCES: Spielman, A. D. (1950), N. Y. St. J. Med., 50:2297, Oct. 1. Brown, E. A., et al. (1950), Ann. Allergy, 8:32, Jan.-Feb. Jenkins, C. M. (1950), J. Nat. Med. Assn., 42:293, Sept. Cullick, Louise, and Ogden, H. D. (1950), South. Med. J., 43:632, July. Ehrlich, N. J., and Kaplan, M. A. (1950), Ann. Allergy, 8:682, Sept.-Oct.



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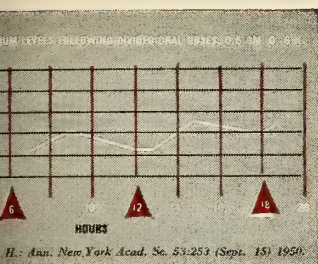
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Ointment, Ophthalmic Solution.*

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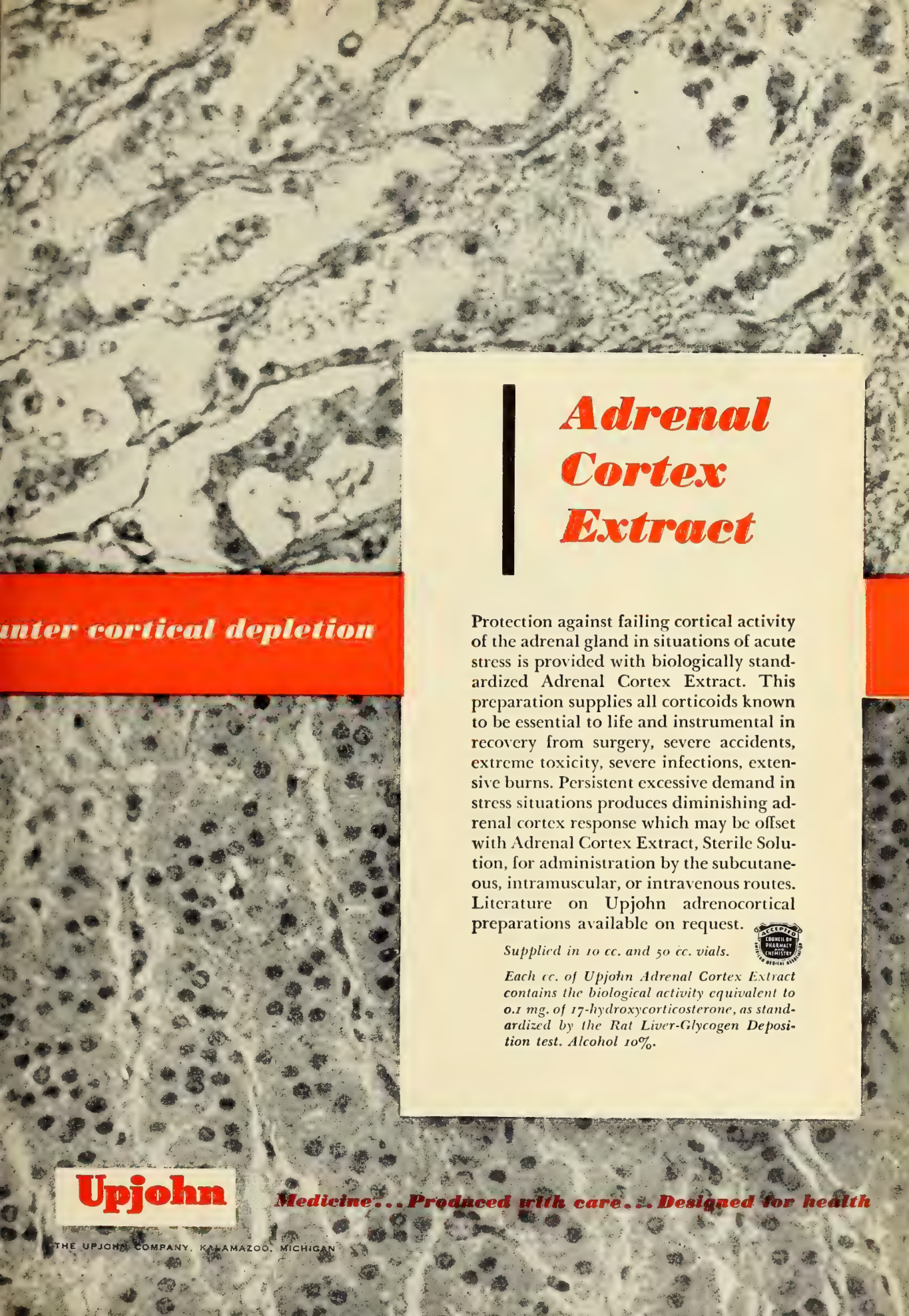
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ORIGINAL ARTICLES

DELAYS IN THE DIAGNOSIS OF TUBERCULOSIS FROM THE INCAUTIOUS USE OF ANTIBIOTICS

W. H. OATWAY, JR., M.D.*

Several years ago the versatile Dr. Walter Alvarez wrote a paper in which he drove home his major point by a series of brief one-paragraph case-reports. Each led to the same obvious conclusion, and the weight of the evidence was great and unforgettable.

It is proposed that the same thing be done in the present report. A discussion and summary will follow, but the evidence is so overwhelming that it will be presented first.

It was recently noted that case-histories of newly admitted patients to a southern California sanatorium included mention of the use of penicillin and other drugs for supposedly non-tuberculous conditions. This often happened without any attempt to exclude or make a diagnosis of tuberculosis.

It was decided to re-check all such information for greater accuracy by questioning the patients. The results were amazing.

Twenty cases is a small number, but the emphasis derives from the fact that the sanatorium contains only fifty beds. *Forty per cent of the patients in residence on February 15, 1951, had suffered to some degree from the 'blind' use of chemotherapy.*—

A—CHEMOTHERAPY WITHOUT AN EXAMINATION FOR TUBERCULOSIS,—

1. A woman, age 25. Two young children in family. 'Cold' with pleurisy for two months, treated with sulfadiazine and *penicillin*. Hemoptysis caused patient to insist on an x-ray. FA exudative lesion found, with cavitation. (Duration of delay . . . 2 months).

2. A woman, age 26. One young child in family. 'Bad cold' treated with *penicillin and aureomycon* for 2 months. Diagnosis by *survey* film. FA exudative lesion with cavity. (Duration of delay . . . 2 months).

3. A woman, age 26. Two young children in family. 'Bronchial trouble' with asthma for 2 years, 'pleurisy' for 1 year. *Penicillin* inhalations at intervals, and for a recent 'cold' Diagnosis finally made by a thorough clinician with gastric culture and G.P. X-ray shows a subminimal lesion. (During of delay . . . 1 to 2 years).

4. A woman, age 29. 'Virus infection' treated with *penicillin* for 2 weeks. Diagnosis made by chance *survey* film) of moderately advanced exudative disease with cavity. (Duration of delay . . . 2 weeks).

5. A man, age 22. 'Pneumonia' with asthma, diagnosed without x-ray 2 years ago, treated with *penicillin*. Diagnosis by *survey* film showed scattered exudative patches with numerous small cavities. (During of delay . . . possibly 2 years).

6. A woman, age 69. Contact with several grandchildren. 'Virus pneumonia' diagnosed 6 months ago but without x-ray. *Penicillin* given until patient got up to care for a sick relative. Diagnosis by *survey* film 3 months later; moderately advanced lesion. (Duration of delay . . . 6 months).

7. A woman, age 38. 'Bad cold' treated with *penicillin* for weeks. Skin-tests had once been negative, so x-ray was not made until a *survey* film was taken, 3 months and 2 doctors later. Lesion moderately advanced.

*La Vina Sanatorium, Altadena, California. (This report was given the Annual Trudeau Award of the California Trudeau Society, April, 1951, and the contest prize of \$150.)

(Duration of delay . . . 6 weeks).

8. A woman, age 36. 'Colds' for 3 months, 'pleurisy' for one week. Therapy with *chloromycetin* for one week. Survey film taken by chance showed FA disease with cavity. (Duration of delay . . . 1 to 3 months).

B. CHEMOTHERAPY, WITH THE TUBERCULOUS LESION MISINTERPRETED,—

1. A male, age 46. 'Bad cold' 18 months ago, treated with *penicillin* injections and inhalations for 2 weeks. X-ray showed patchy lesions, but no further study was made. Survey film showed slight increase in MA tuberculous disease. (Duration of delay . . . 18 months).

2. A woman, age 45. After an accident to her chest 2 years ago, an effusion from trauma was noted, plus a patchy lung lesion. No other diagnosis made. 'Virus pneumonia' the following winter was treated with *streptomycin* because of the patient's sensitivity to *penicillin*. Several courses were given for bronchial symptoms during the next year before a persistent high fever forced a diagnosis of FA tuberculosis with atelectasis and cavity. (Duration of delay . . . 2 years).

3. A woman, age 54. 'Lobar pneumonia' 6 years ago. No x-ray taken, but 'sulfa' was given. 'Virus X', bronchitis occurred 3 years ago, and recurred each winter since. Fluoroscopy was occasionally done. *Penicillin* and (recently) *aureomycin* were used for therapy. The patient continued to work as a nurse. Recent x-rays fell into the hands of a specialist. FA disease was diagnosed with a large cavity and evidence of several bronchogenic spreads. (Duration of delay . . . 3 to 6 years).

4. A woman, age 39. 'Virus infection' 5 months ago, treated with a 'sulfa drug', later with *penicillin*, and finally with *terramycin*. Survey film read as negative. Pleural effusion developed, with tubercle bacilli found by culture and G. P. Earlier films reviewed and seen to contain minimal lesion. (Duration of delay . . . 4 to 5 months).

C. CHEMOTHERAPY IN KNOWN BUT FORGOTTEN CASES OF TUBERCULOSIS,—

1. A woman, age 27. Tuberculosis known to be present for 8 years, but was called inactive. 'Flu' one month ago. *Penicillin*, *aureomycin*, and *terramycin* were tried in order. The occurrence of a pleural effusion resulted in the diagnosis of tuberculous ac-

tivity. (During of delay . . . 1 months).

2. A man, age 36. Tuberculosis known and treated for 4 years, considered to be arrested. Work and emotional strain were followed by 'intestinal flu'. *Terramycin* used for treatment. An hemoptysis resulted in a diagnosis of exudative and cavitative disease. Duration of delay . . . 6 weeks).

3. A man, age 44. Tuberculosis known and casually treated at times for 10 years. Three children in contact. A 'cold' and several 'sore throats' 6 months ago. *Penicillin* therapy was used, but finally stopped because of reactions. An active FA tuberculosis was diagnosed by x-ray later in the year. (Duration of delay . . . 6 months).

4. A woman, age 42. Tuberculosis known to be present for 10 years. 'Virus flu' was diagnosed a year ago, was treated with *aureomycin*. 'Virus flu' 1 month ago, treated with *aureomycin*, was followed by hemoptysis, followed by diagnosis of active FA tuberculosis. (Duration of delay . . . 1 year).

5. A man, age 38. Tuberculosis known and treated 15 years ago. Limited service in the Army Medical Corps. X-rays for 3 life insurance exams read as negative 4 months ago. A 'cold' with bronchitis 2 months ago was followed by bronchitis a month ago. *Penicillin* used for a week, then *aureomycin*. Fever and chill were followed by an x-ray which showed bilateral FA exudative tuberculosis with new cavitation. (Duration of delay . . . 2 to 4 months).

6. A man, age 46. Four children in the family. Tuberculosis first known 6 years ago, when a 'strep throat' was treated with *sulfadiazine* for 4 weeks, relapsed and the lung disease was recognized, treated and arrested. One year ago, after hard work, he felt asthenic and had bronchitis. Rest and some sort of *antibiotic* pills were used. MA tuberculosis was diagnosed when condition did not improve. (Duration of delay . . . 2 to 12 months).

7. A man, age 45. Tuberculosis was diagnosed 10 years ago, treated by San. care and observed since by x-ray. For past year *sulfadiazine* and *penicillin* were repeatedly used for 'bronchiectasis' but no sputum examination was done. More ill 3 months ago, and finally sent to San. with FA fibro-cavernous disease. (Duration of delay . . . 1 year).

8. A woman, age 52. Tuberculosis was

known 14 years ago, treated actively for the first 4 years. A 'virus' Infection two months ago was accompanied by fever, chills, etc. Therapy was *penicillin chloromycetin*, and *aureomycin* was used for 6 weeks, but no x-ray was taken. She returned to work as a nurse, in the nursery of a hospital, but still felt ill. An x-ray finally showed FA disease with a 10 cm. cavity. (Duration of delay . . . 2 months).

DISCUSSION

There are numerous items of interest in this series of cases, and several deductions which can be made.

A free use of antibiotic drugs in cases with respiratory symptoms is bound to include some persons with pulmonary tuberculosis. If an x-ray method is not used, or bacterial studies are not made, these cases will be undiagnosed. Unrecognized cases may progress to a more serious status, and will remain a hazard in contact with family members or other associates.

These things have happened in the cases which have been outlined. They were all infectious at the time of admission to the sanatorium and some of them had become almost untreatable because of the delay and false security given by the use of the antibiotics.

Doctors and patients are alike responsible for the failure to exclude tuberculosis. The patient wants quick and modern treatment; he wants no expensive x-rays; he would cringe away from the idea of tuberculosis if such a thought ever touched his mind. The patient who has had tuberculosis may be just as human, but he is more quilty if he does not insist on a checkup of his lungs when he has an illness with respiratory symptoms. It is his disease and he is partly responsible for it. Too many are ignorant about their own condition, blindly hopeful, and willing to take a chance.

The physician has the duty to be clinically alert for tuberculosis, to use whatever diagnostic measures are needed to exclude it, and to limit chemotherapy to illnesses for which the drugs are useful. He must not overstep the limits of his own type of practice, and should obtain the help of a chest specialist whenever needed. He has no right to prescribe estrogens, 'cold shots', adrenal corticoid substances, iron, vitamin injections (all of which were used in the cases in this series) without an assurance of their need or the absence of tuberculosis. He can take

advantage of free or low-cost x-ray service when the patient is not able to pay for more. He might consider the growing belief that an internist or general practitioner can not practice good medicine without the aid of a fluoroscope.

The chest specialist and sanatorium physician are duty bound to instruct the patient in his future conduct, in the implications of his disease, and in the need for eternal caution, care, and checkups.

The drugs themselves are too alluring, and the reports about them somewhat delusive. Ten years ago a few thoughtful physicians speculated that the sulfonamides might obscure or delay diagnosis of tuberculosis if they were used too casually. The advent of penicillin confirmed that possibility, and patients with neoplasms or tuberculosis came to light at long last when the drugs had 'failed'.

Now we have aureomycin, chloromycetin, terramycin and a probable host of others yet untried. The newer ones become less toxic; the cost is bound to decrease; their use is simplified by oral administration; and they are freely available.

The 'spectrum of activity' is so broad that one is led to believe that pneumonia may be blindly treated, with examination only in case of therapeutic failures. The newer antibiotics are highly effective in coccal and other bacterial pneumonias, in viral, rickettsial, actinomycotic, and other non-bacterial lung infections. Such statements in medical literature or advertising as ". . . the drug of choice in pneumonia, regardless of etiology", and "Once clinical or radiographic diagnosis of pneumonia is made, it is advantageous to start treatment at once, and lose no time waiting for reports of bacteriologic studies", and ". . . there were no cases in which it failed," give too much encouragement. One tends to think of these sentences out of context, and to remove the diagnostic brakes.

A 'broad spectrum' is very fine, but x-ray and bacterial studies are even better.

The 'Duration of Delay' in the cases listed here is only a rough estimate. It might be less in certain cases; it undoubtedly would have been longer in others but for the coincidence of a huge chest x-ray survey which was under way in this area during eight months of the past year. It was a saving factor in several of the cases, as noted; it was a factor in 46 per cent of all cases now in the sanatorium. One shud-

ders when thinking of their fate without the present diagnosis. One hopes for constant and inexpensive x-ray stations for case-finding.

The twenty cases which are reported were fortunate enough to be diagnosed, and are in a small sanatorium. There must be hundreds of similar others in the sanatorium system of the county. There must be thousands in the general public right now whose tuberculous condition is being obscured by non-specific antibiotic therapy. These, and the persons to whom it could happen in the future, are the ones which greater care can protect.

CONCLUSIONS

1. Chemotherapy for lung infections may be hazardous if tuberculosis is not ruled out as a cause of the symptoms.

2. Twenty patients in a small sanatorium of fifty beds have had an appreciable delay in the

diagnosis of tuberculous activity because of the use of chemotherapy and the lack of x-rays, bacterial studies, and clear thinking.

3. The newer antibiotics give a false sense of security because of their broad field of action. The drugs are efficient and attractive, but they must be aimed more precisely at specific and vulnerable infections.

4. The physician and patient both seem to be responsible for the delay in diagnosis, and for a variety of reasons.

5. Persons who have had tuberculosis are especially at fault if they do not check on the cause of lung symptoms.

6. A chest x-ray survey has been especially valuable in helping some of the present patients to a diagnosis. It would be valuable to have inexpensive case-finding facilities constantly available, and physicians would be wise to use them more freely.

THE TREATMENT OF COMMON URINARY TRACT INFECTIONS

ROBERT H. CUMMINGS, M.D.

It has been just 77 years since the specific relationship between microorganisms and infectious disease was first demonstrated in the case of anthrax by Robert Koch. Within the next ten years most of the specific bacteria with which we are familiar today were identified and their specificity demonstrated, according to the postulates laid down by Koch. From that time too, stem the discoveries and the enunciation of the principles and procedures upon which recognition, control, and treatment of all infectious disease is dependent. It is inconceivable that the trained internist today would diagnose typhoid fever without blood culture of Widal reaction, syphilis without serological investigation, subacute bacterial endocarditis without a blood culture, malaria without blood smears, amoebiasis without stool examination and the others too commonplace to mention. Yet, in acute and chronic infections of the urinary tract, diagnosis are made in most cases without, at best, more than an inadequate urine examination.

This is an incongruous situation when one stops to recall the lengths to which one goes to establish the presence of tubercle bacillus in the sputum of the suspected tuberculous patient or positive agglutinations in brucellosis. In every case of urinary tract infection the etiology

may be determined with relatively simple procedures on the urine. In these infections we possess the most ideal opportunity in medical practice to apply specific therapy to accurately identified microorganisms.

In the past ten years we have been privileged to witness the development of chemotherapy and antibiotic therapy, and to enjoy their application. There are evolving, through constant search, forms of therapy specific for even some of the most resistant microorganisms. Yet, in this period of specific therapy, it has been said that pitfalls await the therapist. Seneca, Henderson, and Harvey, in the June 1949 *Journal of Urology* say, "The use of chemotherapeutic agents of any description implies a great clinical responsibility since inadequate or erratic dosage or illadvised choice of any agent is liable to give rise, through natural selection, to daughter strains much more resistant to treatment than the original infecting organism. Hence, a poor therapeutic effort is more than unsuccessful; it is intrinsically harmful."

It is with these two weaknesses in mind, the failure to identify the causative microorganisms and to apply considered specific therapy, that I have prepared these remarks concerning the treatment of common urinary infections. I shall not include tuberculosis, but shall consider com-

mon urinary infections as those pyogenic inflammatory processes of the kidney, ureter, are bladder, manifest by pyuria and bacteriuria.

The symptoms of genito-urinary infection are well known to all and easily recognized. In a like manner, the signs on physical examination need no elucidation. The examination of the urine is of major importance in the management of the patient. The specimen from the female is secured by catheterization in all cases, for by no other means may an uncontaminated specimen be secured. This implies implicitly that a voided urine in the female is valueless. In the male, however, catheterization is unnecessary. Soap and water preparation of the phallus followed by the collection of a portion of the second glass of urine assures an uncontaminated specimen of bladder and kidney urine. The specimen thus secured is studied in the routine manner. The sediment is examined on a wet spread for casts and the number of erythrocytes and leucocytes counted and noted. The wet spread is then air dried, care being taken to avoid heat, because of the real possibility of blasting microorganisms by excessive temperature. After fixing the dried smear by gentle flaming, it is stained by the gram method or for practical ease, by the use of methylene blue. The recognition of microorganisms in every infection is possible and their identification as cocci, bacilli, or both is made. At this point, the definitive treatment of the infection may be initiated but there are three more factors that should be ascertained: 1. The presence or absence of calculi; 2. The presence or absence of an obstructive uropathy of the kidney or bladder outlet; 3. An estimation of the renal function. In the presence of a calculus, it is impossible to eradicate an infection. The same is generally true in obstruction, and in regard to renal function, certain therapeutic substances are contraindicated when impairment is demonstrated.

It is estimated that between 70 per cent to 90 per cent of urinary pathogens are gram negative bacilli; the remainder are gram positive cocci. In reality, both may exist in any one infection and Chittenden of Detroit found 75 per cent of his cases were mixed coccus and bacillary infections. He believes that the presence of bacilli in urinary infection is dependent upon: 1. A prior acute or chronic coccal infection or focus with lowered resistance of the

urinary tract; 2. Structural alteration of the urinary tract such as calculus or obstructive lesions; 3. Accessory genital or adnexal disease. This concept accounts for the frequency of mixed infections and the changing flora noted during the treatment of many protracted infections.

In reviewing the work of several representative investigators, in their series of reported urinary infections, I find that the most common pathogens in urinary infections are *E. coli*, *Aerobacter aerogenes*, *B. proteus*, *Pseudomonas aeruginosa*, *Streptococcus faecalis*, *Streptococcus hemolyticus* and nonhemolyticus, and *Staphylococcus aureus*, and these are the bacteria with which we are most concerned.

The technique of identification of these bacteria is classic and is based upon their colony forms on eosin methylene blue and blood agar plates, their ability to ferment lactose or dextrose with or without acid and gas production, ability to hydrolyze urea, liquify gelatine and produce pigment. The details of this bacteriological identification may be found in standard laboratory texts. It is felt that where bacteriological laboratory facilities are available, this or similar routine identification should be available to all who treat the complicated or protracted urinary infection.

I may not take the time here to discuss sensitivity determinations of isolated bacteria to the several antibiotics. This study is and will become even more important in planning proper treatment of protracted infections.

Prior to the advent of the use of sulfonamides ten years ago, the treatment of urinary infections depended entirely upon the removal of calculi, correction of obstructive lesions, and the alteration of urinary hydrogen ion concentration to produce an environment unfavorable to the growth of the offending organism. Those bacteria producing a strongly alkaline urine were treated by efforts at acidification of the urine and not without some success. However, during this period, two urinary antiseptics were offered representing the first definitive step toward specific therapy; methanamine, an oral medication excreted by the kidney and at a pH of 5.5 freeing formalin in the urine, and mandelic acid, found to be excreted by the normal kidney with urinary antiseptic properties similar to those produced by a ketogenic diet. More recently a salt methaenamine mandelate, known as mandelamine, has been offered. Kirwin reports

83 per cent clinical cures in urinary infections with its use. Carroll and Allen report favorable results in 85.6 per cent of *E. coli*, 71.4 per cent of *Staphylococcus aureus*, and 62 per cent of streptococcus urinary infections, including *Streptococcus faecalis*. Other reports show a comparable result with the use of sulfathiazole, streptomycin, and mandelamine, and they further found that organisms developing increased resistance to sulfathiazole and streptomycin, remained sensitive to mandelamine. This drug is contraindicated in cases of impaired renal function and may cause nausea and dysuria in a few cases. It may be administered as three or four tablets four times daily for several weeks, if necessary. It is most effective against *E. coli*, *Staphylococcus aureus*, and *Streptococcus faecalis*.

The introduction of sulfonamide therapy beginning with sulfanilamide, has marked the advent of definitive treatment of common urinary infections. In rapid succession, all claiming a wide spectrum of effectiveness, have evolved sulfathiazole, sulfadiazine, the intestinal sulfonamides, sulfacetimide now known as sulamyd, and gantrisin introduced as NU 445. Others, which are less commonly used, need not be mentioned but are not ineffective in the hands of many. Most are effective with *E. coli*, *A. aerogenes*, *Staphylococci*, and many beta hemolytic *Streptococci*. To a lesser extent, they are effective against *B. proteus* and *Streptococcus faecalis*. Only *Pseudomonas* is resistant in most strains.

The simplicity of administration and the practical value of the sulfonamides in most urinary infections must be balanced by their serious side effects. The danger of crystal formation and mechanical tubular and ureteral obstruction has been reduced by hydration, alkalization of the urine, and by combining small quantities of two or more sulfonamides. These commercially produced mixtures combine the safety and the solubility of each small quantity component with a high therapeutic effect of the mixture. These combinations and mixtures have nearly replaced the use of sulfathiazole and sulfadiazine alone. In addition to the danger of crystalluria, sulfonamides may produce hyperpyrexia and skin lesions in previously sensitized patients. Agranulocytosis, hemolytic anemia, and lower nephron nephrosis must be constantly watched for by regular blood studies and attention to urinary volume during the period of treatment. The

newer sulfonamides such as Sulamyd and Gantrisin have eliminated the danger of crystalluria but none have eliminated the danger of serious hematopoietic complications with their use.

Sulfathiazole, sulfadiazine, or combinations, are effective against most strains of *E. coli*, *A. aerogenes*, *Staphylococci*, and some strains of *B. proteus* and *Streptococcus faecalis*.

The intestinal sulfonamides, sulfasuxidine, and sulfathalidine control nearly all *E. coli* urinary infections. Their use in pyelonephritis of pregnancy and in recurrent urinary infections have been demonstrated to be practical.

Sulamyd, or sulfacetimide, is effective against *E. coli*, *A. aerogenes*, and many strains of *Staphylococcus aureus*, *Streptococcus faecalis* and *B. proteus*. Toxic reactions, both acute and chronic, are rare and its rapid elimination by the kidney results in low tissue levels. Most important, it is very soluble and crystalluria and anuria probably does not occur. The initial dose is four grams a day for three days then the dose is reduced to three grams daily for seven days, and is given at eight hour intervals.

NU 445 or gantrisin also is well tolerated without toxicity in most cases. It is highly soluble in both acid and alkaline urine so that alkali administration is unnecessary. Intravenous and intramuscular routes may be used. The oral administration of six to ten grams daily for ten to fourteen days is well tolerated and is very effective against *B. proteus*. Gantrisin is also effective against *E. coli* and *Alcaligenes* and *Pseudomonas*. It is ineffective against *Paracolon*, *A. aerogenes*, and *Streptococcus faecalis*.

Penicillin is ineffective against all gram negative bacilli. In spite of this fact, it is probably the most widely used medication in urinary infections. The unconsidered use of penicillin alone in these infections is to be condemned, but, if used together with sulfonamides or other antibiotics, it is entirely acceptable. Penicillin is highly effective against gram negative and gram positive cocci with the exception of *Streptococcus faecalis*. In mixed infections, its use, combined with a sulfonamide, or another antibiotic is necessary although Carroll advises that the gram negative bacilli be eradicated first, before administering penicillin. The oral or parenteral routes of administration may be used and both are equally effective in adequate dosage.

Streptomycin held great promise as a potent antibiotic substance in urinary infections. Its

specific action against many bacteria resistant to sulfonamides and penicillin has been demonstrated. Its value to the urologist is unquestioned. Yet, like penicillin, its ease of administration has led to serious abuses. Streptomycin has been said to be a "one time" antibiotic, in that its readministration in a recurrent or uncured patient is of no value because of the development of resistant strains of bacteria from previous exposure to the agent. It follows therefore that streptomycin should not be administered to a patient with urinary infection until study for calculi or obstructive uropathies has been completed. In fulminating infections of serious magnitude, exception to this rule is justified. But, generally, it is advised that streptomycin be given only to those patients shown to have no correctable anatomical defects of the urinary tract, who do not require catheterization and whose infecting urinary organisms are sensitive in a therapeutic range as determined by *in vitro* studies.

Streptomycin is effective against *E. coli*, *B. proteus*, *A. aerogenes*, and to a lesser extent against *Paracolon* and *Alcaligenes*. It is not effective against *Pseudomonas* or *Streptococcus faecalis*. Four tenths of one gram every four hours will produce blood level of 16 micrograms per milliliter and a urine concentration of over 1000 micrograms per milliliter; a level that will inhibit the growth of most susceptible organisms. The effectiveness of streptomycin is increased at pH 8.0 so that alkalization is advised. Oral administration is valueless in urinary infections.

Aside from the development of resistance in organisms not quickly cured, there are other disadvantages to the use of streptomycin. In usual therapeutic doses, it is practically non-toxic. In larger dosage or after continued use, side reactions of varying severity may occur and are well known to all. These side reactions may be reduced by the use of dihydrostreptomycin without altering the clinical effect.

Aureomycin, introduced in 1948, has proven to be a versatile urinary antibiotic administered either intramuscularly or orally. Peak concentration occurs in three hours after intramuscular injection, and the optimum interval by oral route is three hours for 250 mgm. or six hours for 500 milligrams. The urinary concentration is 100 times that of the serum and it produces an acid urine where its effectiveness is increased.

Aureomycin is most effective against *E. intermedium*, *E. coli*, *A. aerogenes*, *paracolon*, *alkaligenes*, and *Strep faecalis*. Also sensitive are *B. hemolytic Streptococci* and *Staphylococcus aureus*. No sensitivity is shown by *B. proteus* and *Pseudomonas*. Aureomycin resistant strains do not develop and its repeated use is therefore possible. There is generally no evidence of toxicity to its use although patient allergy may be developed following repeated use. Nausea following ingestion is not uncommon but is reduced by administering the medication with allumina gels or buttermilk.

Chloremycetin, isolated from *Streptomyces venzuellae*, has now become the first antibiotic to be synthesized. It is well tolerated without toxic or side reactions. It is rapidly absorbed by oral or rectal routes. The dosage is 50 mgm. per kilogram for the acute days of the infection; then reduced in half for periods of five to seven days. Chloromycetin is effective against *E. coli*, *A. aerogenes*, and *proteus*. Also it is effective against *Staphylococci* and *Streptococci*. No effect against *pseudomonas* infections is again noted.

Polymyxin is mentioned here, although its clinical application is as yet premature. Its importance lies in the fact that, other than mandelic acid and mandelamine, it is our only therapeutic measure effective against *pseudomonas* infections. This antibiotic is derived from *B. polyxa* and is very soluble, being administered only by the intramuscular route. The dosage is 2.5 milligrams per kilogram of body weight. With this dosage there is little renal tubular damage or elevation of the blood urea nitrogen. Administration is at six hour intervals for three days. All patients, however, develop neurotoxic reactions such as paraesthesias, hypaesthesias, dizziness, and weakness. Polymyxin is effective against *E. coli*, *A. aerogenes*, *paracolon*, and *Staphylococci*. It is less effective against streptococci and useless against *B. proteus*.

Following this rapid and sketchy review of our therapeutic armamentarium, the management of a common urinary infection may be discussed.

In those patients without a previous history of urinary infection, it is sufficient to base the therapy upon the finding of bacteria in the stained sediment of the urine. If gram negative bacilli are found, a sulfonamide, such as sulfadiazine, sulfathiazole, or mixtures, in dosage of

0.5 grams every six hours is prescribed for seven days, with adequate fluid intake and alkalinization used. If gram positive cocci are found, together with the bacilli, penicillin is also given. At the end of one week, the urinary sediment is again examined and if free of pyuria and bacteriuria, it is but necessary to examine the urine for two weeks to be certain recurrences do not occur. Should the infection promptly recur or should the checkup reveal that pyuria persists, cystoscopy and retrograde pyelography is indicated, and at that time, the bladder and ureteral specimens are examined to locate the source of the pyuria and cultured to identify the causative organisms. If sensitivity studies can be made, the appropriate antibiotic can be determined. Should calculus or obstruction be discovered, streptomycin should be withheld until the basic pathology has been corrected. During the period of preparation for surgery, other effective antibiotics or sulfonamides, if indicated, may be used.

In those patients who have had repeated infections of the urinary tract, one may save time by performing cystoscopy and retrograde pyelography with urine cultures at the onset for there is generally a predisposing cause for chronic pyuria.

During the period of specific therapy urinary sediment bacteriology must be repeatedly studied because of the change of flora in resistant mixed infections. Furthermore, in sulfonamide and streptomycin therapy, changes in sensitivity of microorganisms are commonly found, necessitating a change to an effective agent.

Where it is not possible to do sensitivity studies, specific treatment may be based upon a knowledge of effective therapeutic agents for the various urinary pathogens. These may be summarized as follows:

B. coli: most effective are mandelamine, gantrisin, sulamyd, aureomycin, chloromycetin, and streptomycin where its use is not contraindicated. The drugs of choice are streptomycin, aureomycin, and chloromycetin. If long periods of therapy are necessary, the sulfonamides: gantrisin, and sulamyd and mandelamine are recommended.

E. intermedium: This organism is probably of importance only when suspected *E. coli* infection is not promptly cleared with streptomycin. Aureomycin is the drug of choice.

A. aerogenes: this increasingly important secondary invader responds to sulamyd, aureomycin, chloromycetin, and streptomycin, with aureomycin or chloromycetin first choice.

Paracolon: chloromycetin is the antibiotic of choice with sensitivity also noted to streptomycin.

B. proteus: this important urea splitting organism shows strains sensitive to most sulfonamides with sulamyd and gantrisin most effective. Many strains also respond to streptomycin and to chloromycetin. Aureomycin is not recommended since these urines show an alkaline hydrogen ion concentration.

Pseudomonas aeruginosa: this organism was formerly considered harmless. Recently the urologist has come to look upon it as a producer of infection of major significance. The antibiotics are useless except for polymyxin and the safe use of this agent remains somewhat in the future. Mandelamine is the drug of choice and all sulfonamides should be tried.

Alkaligenes: gantrisin and aureomycin are the recommended agents and some strains are sensitive to streptomycin.

Streptococcus faecalis: this enterococcus is a common pathogen, especially in the paraplegic patient. Penicillin is of no value and streptomycin is effective only in a few strains. Furthermore, where reinfection is common, streptomycin is not recommended except in fulminating infections. Mandelamine is very effective, sulamyd is the sulfonamide of choice and aureomycin and chloromycetin are the antibiotics of choice.

Streptococcus hemolyticus: the beta hemolytic organisms are sensitive to sulfonamides. Both alpha and beta hemolytic streptococci are sensitive to penicillin, aureomycin and chloromycetin, with penicillin being recommended.

Streptococcus nonhemolyticus: penicillin is recommended.

Staphylococcus aureus: Many therapeutic agents are effective, including mandelamine, sulfonamide mixtures, sulamyd, aureomycin, and chloromycetin, but most important is penicillin.

In conclusion, three rules of treatment for common urinary infections are offered:

1. Properly collect a urine specimen and identify a causative organism in the sediment before initiating treatment.

2. Investigate recurrent and chronic urinary infections for organic urinary pathology.
3. Utilize a therapeutic agent that shows

effectiveness against the infecting organism or which statistically has a chance of being of value.

SURGICAL JAUNDICE

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Perplexing situations arise in the analysis of the causes of jaundice. Whether because of insufficient study, or equivocal or contradictory laboratory data, some patients with obstructive jaundice are not treated surgically. It has been facetiously stated that the great value of the many liver function tests is in the time it requires to perform them, during which the patient may be carefully examined and studied. In a sense this is so, as the daily fluctuation, or its absence, in the intensity of the jaundice or acholia maybe nearly as important in reaching a diagnosis as the history, examination and other laboratory data.

Jaundice results from the retention of bilirubin in the blood stream. Bilirubin is formed from the iron free pigment (hematoidin) of the erythrocytes by the reticulo endothelial cells, and is secreted by the liver in bile. The bilirubin is delivered to the intestines, where by enzymatic activity, it is converted to urobilin. The greater part of this passes out of the body in the stool, giving the stool its characteristic color. Some of the urobilin is delivered again to the liver via the portal system by resorption from the intestine. The liver reconverts some of it to bilirubin.

For practical purposes jaundice may be considered to be hemolytic or prehepatic, hepatocellular or intraphepatic, and obstructive or extrahepatic. In hemolytic jaundice excessive hemolysis of erythrocytes occurs, usually with normal liver function. Thus increased bilirubin is formed giving rise to increased urobilin in intestines and feces. The excess amount of urobilin returned to the liver cannot all be reconverted to bilirubin and spills over in the urine in large amounts. In intrahepatic jaundice excessive spill of urobilin does not occur. In obstructive jaundice inasmuch as little or no bilirubin reaches the bowel fecal and urinary urobilin may be low or negligible.

Differentiation of obstructive from hepatocellular jaundice may be exceedingly difficult. Every physician with extensive experience can bring to mind instances of both types of jaundice in why atypical findings have been present. By and large obstructive jaundice is characterized by seldom presenting in its early phases, at any rate, signs of disturbed hepatic function, and will present symptoms of interference with biliary flow. Painful colics, transient or permanent acholia, retention of biliary products other than bilirubin, and decreased to absent urinary and fecal urobilinogen may be encountered. On the other hand primary hepatic jaundice generally does not show interference with biliary flow into the intestine beyond four or five days, and does show early definite evidence of liver dysfunction.

Reasonable proof of mechanical biliary obstruction should be present before subjecting the jaundiced patient to surgical treatment. The obstruction may be partial or intermittent, as well as complete. If a good history can be elicited of gall stones, of colic, of recurrent biliary obstruction with fever with or without pain, of jaundice following cholecystectomy or of post-operative biliary fistula, there is excellent indication for surgical treatment. Likewise a palpably distended gallbladder, and proved complete and permanent acholia are absolute indications. In all of the above instances liver function should be normal, or compatible with the duration of the jaundice.

There is no absolute protection as yet available against the possibility of occasionally employing surgical therapy where it may be inadvisable, in some instances of chronic hepatitis, cholangitis, compensated cirrhosis and chronic relapsing pancreatitis. In the presence of the following warning signs or symptoms or findings, surgical exploration should be utilized only after due study and thought. One rarely encounters edema, or evidences of collateral circulation, or low serum proteins and reversed albumin-glo-

bulin ratio in obstructive jaundice. A reliable episode of exposure to hepato-toxic agents, to plasma or blood transfusion within sixty to one hundred-twenty days, rather suggests intra-hepatic jaundice. Chronic jaundice with splenomegalia, and hemolytic activity are not usually seen in obstructive jaundice. Feter hepaticus indicates rather cirrhosis or hepatic atrophy. Intense jaundice with unobstructed biliary passages fits in with primary carcinoma of the liver or severe hepatic necrosis. Finally reduced cholesterol and cholesterol esters under fifty milligrams per cubic centimeter of plasma indicates severe liver damage, as does failure of hippuric acid synthesis and hypoprothrombinemia refractory to Vitamin K.

A multitude of tests may be employed in an effort to determine whether a given patient's jaundice is due to extra-hepatic obstruction or otherwise. It not infrequently results that contradictory or equivocal findings add confusion rather than shed light on the problem. The use of duodenal drainage has been advocated but is so highly inaccurate as to be relatively valueless unless blood is found on the drainage. The Schmidt test for bile in the stool may be misleading, and result in negative findings when there is merely low bilirubin content in a bulky stool. The use of the Graham-Cole X-ray in the presence of deep jaundice may be meaningless when non-visualization occurs as ordinarily results. A flat roentgen plate of the abdomen may show opaque calculi in the region. In the last analysis the best proof of biliary obstruction lies in the findings of absent or very low values of fecal and urinary urobilinogen. Suggestive findings of biliary obstruction in the blood of the jaundiced patient would be elevation in the alkaline phosphatase and cholesterol and cholesterol esters.

It is imperative that some studies of liver function be performed in the jaundiced patient if mistakes are to be kept to an absolute minimum, for the liver function should be normal or compatible with the duration of the jaundice in those instances which may be benefited by surgical therapy. The cephalin cholesterol flocculation of Hanger and the thymol turbidity tests are very sensitive liver function tests and if they are highly positive great caution should be exercised before recommending operative treatment. The bromsulphalein excretion test is valueless in the presence of jaundice. In most

obstructive jaundices the serum protein, albumin-globulin ratio, and hippuric acid secretion should be normal. Finally a prompt return to normal of prolonged prothrombin time upon the administration of Vitamin K, should occur in the patient where jaundice is due to obstruction. Conversely in intraphepatic jaundice the following are expected: normal alkaline phosphatase, normal or low cholesterol and cholesterol esters, reduced serum protein, reversed albumin-globulin ratio, positive thymol turbidity and cephalin flocculation, decreased hippuric acid secretion, and delayed or absent response to Vitamin K administration.

In the last analysis no amount of scientific data can replace accurate clinical acuity and judgment in the jaundiced patient. If after careful study the cause of jaundice is felt to be obstructive then surgical therapy may be employed after adequate preparations to correct hypoprothrombinemia, hypoproteinemia, hypovitaminosis, anemia, and glycogen depletion. A plea should be made for not lingering too long in reaching a diagnosis and using surgical treatment in those patients who have chills and high fever with obstructive jaundice as some of these patients rapidly develop overwhelming liver infection with multiple abscesses which cannot always be successfully controlled even after relief of obstruction. Finally it should be remembered that jaundice occasionally occurs in amebiasis and ulcerative colitis. These conditions should be excluded where there is any question of their presence before undertaking operative intervention.

The following somewhat abbreviated two examples have been selected to illustrate some of the above points.

1.) C.C.—48 year old, single, Spanish-American male janitor, entered the hospital with a complaint of mild epigastric discomfort relieved by alkalies for three weeks, severe right upper abdominal colic radiated to the back with nausea for nine days, jaundice with light stools and dark urine for eight days. Seven pounds of weight were lost in this period. He admitted taking three bottles of beer and one whiskey shot daily for years, and stated he used to drink heavily. No plasma or blood transfusions had ever been administered him. He admitted gonorrhea ten years before.

Essentials of his examination revealed an afebrile, jaundiced male of the stated age, with

carious teeth, a firm moveable tumor of the occiput 3x4 cm. with no abnormalities except a palpable mass considered to be liver extending four fingers below the right costal margin. One observer felt questionable nodules in the mass. The rectal examination revealed alcoholic stool on the glove.

Laboratory examination revealed 13.9 grams of hemoglobin per 100 c.c.; 4,500,000 r.b.c.; 7,800 w.b.c. per cum. mm; normal differential. Urine normal, except for showing positive test for bile, and urobilinogen. Kahn was negative. Cephalin flocculation was negative. Stool showed no parasites or ova. Icteric index was 60 units. Serum protein was 7.0 grams per 100 c.c. with 3.6 grams albumin and 3.4 grams globulin. Prothrombin time was patient 19 seconds control 16 seconds or 84% of normal. Two days later urobilinogen was weakly positive 1:10. Four days later icteric index was 120 and urobilinogen in the urine was negative. Twelve days later the icteric index was 140, urobilinogen in the urine was still negative, and cephalin flocculation showed 1+ in 48 hours. Flat plate of the abdomen was negative.

In this patient then without previous history suggestive of biliary disease, *very* deep jaundice is seen with normal liver function, as demonstrated in the cephalin flocculation and serum protein and albumin-globulin ratio tests. Proof of total biliary obstruction and over a period of at least eight days is present in the absence of urobilinogen in the urine. The very high icteric index would suggest primary liver carcinoma. Operation revealed multiple whitish-hard nodules throughout the entire liver, biopsy of which showed biliary duct carcinoma of the liver. There were widespread metastases on the omentum and peritoneal surfaces. The gallbladder was greatly distended and contained stones, one of which was impacted in the cystic duct. Palliative cholecystogastrostomy was performed, jaundice was not relieved. The patient recovered from the operation to die one month later from carcinomatosis.

Somewhat more puzzling was the situation with

2.) I.A.—40 year old, single, Spanish-American, farm laborer, entered the hospital with a complaint of epigastric fullness and distress with nausea and undetermined amount of weight loss of six months duration. For one month he had constant epigastric distress, and jaundice without

itching of the skin, but with light stools and dark urine for two weeks.

Examination revealed a chronically ill, deeply jaundiced male with temperature of 101.8°. Except for a moderately distended abdomen with marked tenderness over the epigastrium nothing significant was found on physical examination. The liver could not be felt, no masses could be felt, and no shifting dullness could be demonstrated. Alcoholic stool was demonstrated on the rectal glove.

Over a seventeen day period extensive laboratory studies were made, during which time the patient's temperature fluctuated between 101° and 104° daily with chills. Admission hemoglobin was 11.65 grams per 100 c.c.; r.b.c; 3,987,000 per cu. mm; w.b.c. 15,600 per cu. mm. of which 95% were polys, 5% lymphocytes. Icterus index was 50 U, 50 U and 40 U in this period. Prothrombin time was 64% of normal, and after four days with Vitamin K administration was still 64% of normal. N.P.N. was 30 mgs. per 100 c.c. of blood. Urine was positive for bile and showed positive for urobilinogen in 1:80 dilution. Alkaline phosphatase showed 17.3 units by King Armstrong method. Cholesterol of the blood was 243 mgms. per 100 c.c. blood. Amylase was 42, 25 and 38 mgm. per 100 c.c. blood. Serum albumin was 4.10 grams per 100 c.c. blood and globulin 2.00 grams per 100 c.c. blood with a total protein of 6.10 grams per 100 c.c. of blood. The albumin-globulin ratio was 2.051. There was no free HCl in the stomach. Stools were negative for parasites and ova. Blood cultures were negative. Na malarial parasites were seen on smears. Agglutinations for typhoid, paratyphoid, proteus X and Brucella were negative. There was no response to emetine hydrochloride. The Kahn was negative.

In this patient then conflicting data are present. A rather constant jaundice level is seen of 40 to 50 icteric index units, although clinically it seemed more intense. Some evidence of liver damage is seen in a two plus cephalin flocculation test, elevated alkaline phosphatase, and failure of response of prothrombin time upon administration of Vitamin K. Yet serum proteins and albumin-globulin ratios were normal, as was serum cholesterol. Obstruction could not have been complete with urobilinogen still in the urine. X-rays not previously mentioned showed non-functioning of the gallbladder, as would be expected with this degree of jaundice,

and the gastrointestinal series was negative. Chest X-ray showed chronic fibrous pleuritis of the right base, with calcifications of the left lung field. An electrocardiogram showed only non-specific myocardial damage.

In spite of the conflicting laboratory findings clinically the patient seemed to have obstructive jaundice without evidence of cirrhosis and the medical consultant made a diagnosis of obstructive jaundice due to carcinoma of the pancreas. The surgical consultant made a diagnosis of obstructive jaundice probably due to carcinoma of the liver, gallbladder or pancreas.

At the operation, after careful preparation with transfusions, etc., a greatly distended gallbladder and common duct the size of a silver dollar were found. The pancreas was normal. Opening of the common duct failed to reveal the cause of the obstruction at the Ampulla of

Vater. Transduodenal exploration then revealed a 1½ cm. in diameter adenocarcinoma of the Ampulla of Vater without gross evidence of metastases.

Despite adequate relief of biliary obstruction the patient succumbed in twenty days from cholangitis, minute liver abscess, and bronchopneumonia. This occurred even in spite of vigorous use of antibiotics, pre and post-operatively and serves to illustrate the need for early relief of jaundice due to obstruction with patients having chills and high fever.

In conclusion:—patients with true obstructive jaundice should be treated surgically, and, at a time as early as possible after an accurate diagnosis is made and proper preparation completed. If complications such as cholangitis and liver damage are to be kept minimal.

BASIC SCIENCE SEMINAR

**PIMA COUNTY GENERAL HOSPITAL
TUCSON MEDICAL CENTER — ST. MARY'S HOSPITAL
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PHARMACOLOGY OF DIGITALIS & RELATED COMPOUNDS

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Digitalis and certain closely related drugs have in common a specific and powerful action on the myocardium which is unrivaled in value for the treatment of heart failure. These cardiac drugs are mainly of plant origin but are also present in the cutaneous secretions of certain toads. The preparations commonly used are obtained from three groups of plants; the foxglove or digitalis group, the strophanthus group, and the "sea onion" or squill group.

HISTORY

As is true of many valuable modern drugs, the cardiac glycosides were probably first used to kill rather than to heal. At least many of the plant extracts used by natives in various parts of the world as arrow and ordeal poisons contained cardiac glycosides. However, the ancient Egyptians knew squill as a medicine as early as 1500 B. C., and the Romans employed it as a diuretic heart tonic, and emetic; as well as a rat poison. Strophanthus was introduced into medicine by Sir Thomas Fraser in 1890 who discovered its

digitalis-like action while studying African arrow poisons. A drug which has been used for centuries by the Chinese is the dried skin of the common toad. Powdered toad skins were also commonly employed in the folk medicine of western countries for dropsy until replaced by digitalis.

Digitalis or foxglove was mentioned as early as 1250 in the writings of Welsh physicians and was described botanically by Fuchsius in 1542. Fuchsius gave it the name *Digitalis purpurea* because the flower was purple and resembled a finger. For two hundred and fifty years more, foxglove was occasionally used internally or locally for a number of unrelated diseases ranging from epilepsy to skin ulcers.

It remained for William Withering, master physician and botanist of Birmingham, England to recognize and record the specific pharmacological actions of digitalis. And if it hadn't been for Withering's unusual interest and broad knowledge of botany the discovery of digitalis as a

specific for cardiac failure may have waited another few centuries. It seems that, and I quote from Withering's famous monograph on the subject, "In the year 1775, my opinion was asked concerning a family receipt for the cure of the dropsy. I was told that it long had been kept a secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed. I was informed also, that the effects produced were violent vomiting and purging; for the diuretic effects seemed to have been overlooked. This medicine was composed of twenty or more different herbs; but it was not very difficult for one conversant in these subjects, to perceive, that the active herb could be no other than Foxglove."

Withering apparently knew that digitalis was effective only in certain forms of dropsy or edema for he also wrote:

"Independent of the degree of disease, or of the strength or age of the patient, I have had occasion to remark, that there are certain constitutions favourable, and others unfavourable to the success of the Digitalis."

"From large experience, and attentive observation, I am pretty well enabled to decide upon this matter, and I wish to enable others to do the same; but I feel myself hardly equal to the undertaking. The following hints, however, aiding a degree of experience in others, may lead them to accomplish what I yet can describe but imperfectly."

"It seldom succeeds in men of great natural strength, of tense fibre, of warm skin, or florid complexion, or in those with a tight and cordy pulse."

"If the belly in ascites be tense, hard, and circumscribed, or the limbs in anasarca solid and resisting, we have but little to hope."

"On the contrary, if the pulse be feeble or intermitting, the countenance pale, the lips livid, the skin cold, the swollen belly soft and fluctuating, or the anasarcaous limbs readily pitting under the pressure of the finger, we may expect diuretic effects to follow in a kindly manner."

Although Withering observed that digitalis was effective only in certain forms of dropsy he apparently did not associate this with the cardiac action of the drug. He recognized that the heart was affected, however, for he wrote that, "It has a power over the motion of the heart to a degree yet unobserved in any other medicine, and this power may be converted to

salutary ends." Apparently John Ferriar in 1799 was the first to ascribe to digitalis a primary action on the heart and to relegate the diuretic effect to a secondary role.

Whereas Withering knew and recorded the benefits to be derived from the proper use of foxglove, his advice was not always taken. During the 19th century, digitalis was used indiscriminately, often in toxic doses, for many disorders. During the early 20th century, as a result of the work of Cushuy, Mackenzie, Lewis and others, the drug gradually came to be looked upon as a specific in the treatment of auricular fibrillation. Only within the last 20 years has it become firmly established that the main value of digitalis is in the therapy of congestive heart failure.

SOURCE AND COMPOSITION OF THE CARDIAC GLYCOSIDES

In Withering's time little or nothing was known of the specific active compounds contained in the foxglove and other related plants that gave them their observed pharmacological actions, and even today official digitalis is still designated as the dried leaf of the foxglove plant *Digitalis purpurea*, the flowering biennial common in many parts of the United States. However, other members of the digitalis species contain the same compounds and other active cardiac principles as well. The foremost of these is *Digitalis lanata*.

Official *strophanthus* is obtained from the seeds of the *Strophanthus kombi*, while *Ouabain* is derived from *Strophanthus gratus*. Belonging to the same family is a tropical tree, the common name of which is the yellow oleander, that produces a fruit known as the bestill or Malayan nut. The kernel of this nut yields the active cardiac principle thevetin.

Official squill comes from the dried fleshy bulb of the "sea onion", *Scilla Maritima*.

Many other plants contain digitalis-like compounds, but they will not be considered in this paper because their clinical value has not yet been fully established.

The active compounds contained in all these cardiac drugs are glycosides and are closely related chemically. Each glycoside is made up of an aglycone or genin together with one or more molecules of a sugar. The pharmacological activity is in the aglycone, but the particular sugars to which the aglycone is attached is thought to control water solubility, cell pene-

SOURCE AND COMPONENT CHEMICAL PARTS OF THE
MAJOR CARDIAC GLYCOSIDES

Source		Glycoside	Sugar	Aglycone
Digitalis	Purpurea	Deacetyldigilanid A —Glucose=Digitoxin	3 Digitoxose	Digitoxigenin
	Leaves	Deacetyldigilanid B —Glucose=Gitoxin	3 Digitoxose	Gitoxigenin
		Gitalin	2 Digitoxose	Gitaligenin
	Seeds	Digitalin*	Glucose and Digitalose	Digitaligenin
Digitalis	Lanata	Digilanid A —Glucose —Acetyl =Digitoxin	3 Digitoxose	Digitoxigenin
	Leaves	Digilanid B —Glucose —Acetyl =Gitoxin	3 Digitoxose	Gitoxigenin
		Digilanid C —Glucose —Acetyl =Digoxin	3 Digitoxose	Digoxigenin
	Strophanthus S. Gratus S. Kombe	Quabain K-Strophanthin K-Strophanthoside	Rhamnose Glucose and Cymarose 2 Mol. Glucose and Cymarose	Quabagenin Strophanthidin Strophanthidin
Squill		Scillaren A	Glucose and Rhamnose	Scillaridin A

*Not commercial "Digitalin".

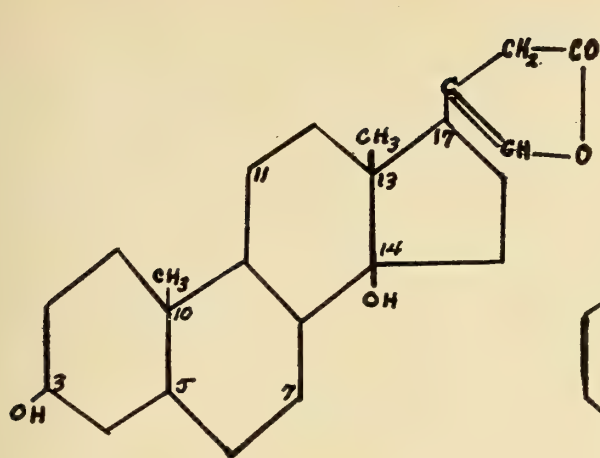
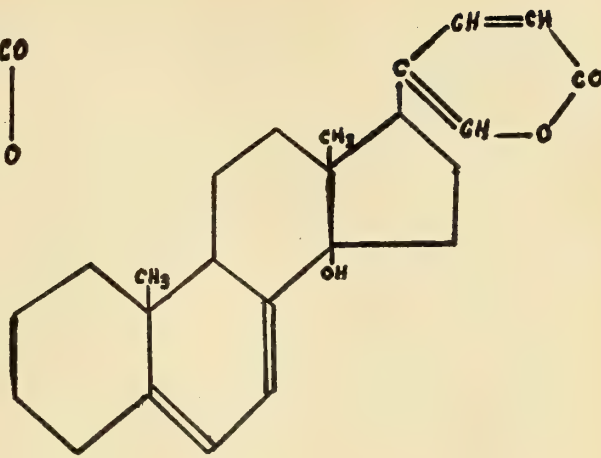
FIGURE 1

trability, and persistence of cardiac action; therefore, the therapeutic potency of the molecule. For example, the sugars are inactive when given alone, but when linked to aglycones the potency and toxicity of the aglycones are increased several fold. All of these sugars are monosaccharides. Some are well known, such as glucose and rhamnose. Others, such as digitoxose and digitalose, are unusual pentose sugars which are found only in the digitalis glycosides and are unlike any known sugars. The following table (Figure I) indicates the source and component chemical parts of the major cardiac glycosides.

Rapid advances have been made in recent years in the complicated chemistry of the cardiac aglycones. They can be released from the cardiac glycosides either by acid or enzymatic hydrolysis. Their complex structure was but poorly understood until it was discovered that they are chemically related to the bile acids, cholesterol, sterols, and sex hormones. The

basic structure is a clyclopentenophenanthrene nucleus to which is attached a lactone ring. Methyl, hydroxy, and aldehyde groups are also attached in specific positions, varying with the particular aglycone. The empiric formula is usually $C_{23}H_{34}O_{(4-8)}$. In order to show the close structural relationship between the molecules of the different aglycones, the structural formulas of digitoxigenin and scillardini-A will be demonstrated (Figure 2).

Other important aglycones differ structurally from digitoxigenin and scillaridin-A only in minor ways. Gitoxigenin, which is found in digitalis leaves with digitoxigenin, differs from digitoxigenin only in having an hydroxy group at C₁₆. Strophanthidin is different from digitoxigenin only by an hydroxy at C₅ and an aldehyde group at C₁₀ in place of a methyl radicle. Digoxigenin, a third digitalis aglycone found in the Digitalis lanata species has the same carbon skeleton but it also has a third hydroxy group the position of which has not definitely

**DIGITOXIGENIN****SCILLARIDIN-A**

been determined. Ouabagenin, from ouabain, has the same structure as digitoxigenin except for a $\text{C}_2\text{H}_5\text{O}$ group instead of C_2H_5 on C_{10} and hydroxy groups on C_7 and C_{11} . It can be seen that Scillaridin A, the aglycone of squill, differs from the aglycones of the digitalis-strophanthus group in having an extra C atom. This carbon is in the lactone ring and makes scillaridin-A the intermediate link between the cardiac glycosides and the bile acids.

With many drugs a slight variation in the chemical structure causes marked changes in the pharmacological actions, but so far as is now known this doesn't seem to be true for the cardiac glycosides. Apparently they all produce the same type of cardiac effect, but practically nothing is known of the basic mechanism whereby the effect is produced. It appears that the glycosides enter the cell protoplasm and are there split to release the active aglycones.

CARDIOVASCULAR ACTIONS

It seems unusual that a drug which has been known and used for centuries can still cause so much controversy as to its major site of action, but this is the case with digitalis. There is some disagreement at the present time whether the primary action of digitalis-like compounds is on the myocardium of the heart or on the blood vessels. Some competent workers maintain that the primary action of digitalis is to lower the venous pressure and by this means remove the venous congestion of the failing heart and allow it to recover its efficiency. It is claimed that the site of action of therapeutic doses is on the peripheral vessels, in particular

on those of the liver. Digitalis is said to constrict the smooth muscle in the hepatic vein, pool the blood in the liver and portal system, relieve the right side of the heart of the overdistention caused by venous congestion, and in this manner improve cardiac function. Only toxic doses of the glycoside are admitted to be capable of action directly on the heart, and then only to decrease the efficiency of the heart so far as cardiac output is concerned. Evidence in support of this interpretation has been obtained especially in experiments on the dog (Dock and Tainter, 1930; Katz and collaborators, 1938). The work of McMichael and co-workers in 1944 and 1946 also suggested that the primary action of digitalis was on the great veins. All of these experiments, (with the exception of those of McMichael and co-workers), were carried out on the dog and assume that digitalis acts on the hepatic veins of man as it does in the dog.

There are, however, many observations against this interpretation. First, according to most observers, heart failure is the cause rather than the result of increased venous pressure. Secondly, the venous pressure in marked congestive failure is insufficient to be a factor in stretching of the right ventricle. Thirdly, in isolated left ventricular failure, digitalis causes restoration of compensation without significant change in venous pressure. Fourthly, digitalis causes a decrease in the size of the swollen liver in congestive failure rather than an increase which is necessitated by the above theory. Fifthly, the amount of smooth muscle in the hepatic veins

of man is quite sparse and forms no distinct sphincter as does the more abundant smooth muscle in the dog.

Finally, what seems to be the decisive blow to the peripheral vascular theory was struck by the work of Ferrer and co-workers in 1949. In this study a double lumen catheter was introduced so that one lumen rested in the pulmonary artery and the other in the right ventricle. Under carefully controlled conditions the changes in pressure in the right ventricle and pulmonary circulation was measured before and after digitalization in five patients with pure left sided heart failure. Digoxin, the digitalis preparation used, produced a significant rise in cardiac output and stroke volume accompanied by a decrease in pulmonary arterial pressure in each of these five patients. These changes were effected without alteration in the right ventricle end diastolic pressure, thus leading to the conclusion that in man at least the primary site of action of the drug was on the myocardium and not upon the systemic venous system.

It seems inescapable from the above observations in man and from observations on strips of heart muscle, in isolated mammalian hearts, in heart-lung preparations, and in experiments of various types in intact animals that digitalis acts on the myocardium to make it work more efficiently. But even though it is at the present time the general consensus of opinion that digitalis does act directly and primarily on the myocardium, there are two major schools of thought as to how it acts on the muscle fibers. One school believes that digitalis shortens the diastolic length of the muscle fiber, thus increasing the muscle tone and therefore the efficiency. This school minimizes the idea of an increase in force of systolic contraction. Stewart and Cohn have been the major exponents of this theory of action. In a recent article Stewart states as follows:

"It is my notion that the human heart observes to a large extent Starling's Law: with dilation of the heart and increase in length of muscle fibers, the cardiac output first increases; as stretching proceeds farther, the lengths of muscle fibers exceed their optimal length and the cardiac output now falls off. One explanation of the observed effects of digitalis on the large dilated failing heart is as follows: Digitalis exerts an effect on lengths of muscle fibers; namely, decreases them, and the summated effect on all

fibers is to make the heart a smaller pump. The consequence in the normal person is for digitalis to make the heart smaller, in fact too small, so that the cardiac output decreases since the pump is smaller. In the failing, dilated heart the shortening of the stretched fibers makes them approach more nearly an optimal length, the heart decreases in size and the cardiac output increases. In this notion we think the effect on heart size is crucial."

"Everyone of these effects can be easily demonstrated in man from the use of therapeutic amounts of the drug."

"In strips of cat heart muscle another effect of digitalis can be demonstrated, namely an increase in force of contraction. This effect no doubt contributes to the benefit of the drug but it cannot be the main effect, because it would also increase the cardiac output of the normal heart as well as the failing one."

In contrast to the above, Gold and co-workers, and others hold that digitalis bodies are effective in heart failure not by increasing cardiac tone as claimed by Stewart and Cohn and their associates, but by improving the strength of systolic contraction. Their experiments on papillary muscles and tortoise hearts indicate that digitalis enhances the force of systole without a decrease in diastolic length and throughout a wide range of diastolic lengths. However, with present x-ray techniques it can be shown that the human failing heart does decrease in size after digitalization, and this also seems to be true with normal hearts. Therefore, in view of the evidence on both sides, it seems best in the light of our present knowledge to conclude that digitalis does act primarily on the heart muscle to decrease its diastolic size and to increase the force of systolic contraction.

The idea that digitalis always increases the force of systole does not seem to stand up when one considers the fact that the cardiac output of the normal human heart is decreased from 20 to 35 per cent by digitalis. It looks as if the output should increase with increased force of contraction. However, if we remember that the diastolic size of the normal heart is decreased by digitalis, it becomes apparent that even though the heart muscle contracts more forcefully it is possible for it not to force out as much blood because, due to its decreased size, it doesn't contain as much blood as normally. The cardiac output is also dependent

upon the heart rate, stroke volume, velocity of blood flow, peripheral resistance, and venous return. The important fact remains that digitalis decreases the cardiac output in normal hearts but increases it in failing hearts.

Digitalis also decreases the venous pressure if it is increased as a result of congestive heart failure. A fall of pressure from 20 cm. of water to 5 cm. within 24 hours is not unusual. This decrease in venous congestion is most probably secondary to the improvement which occurs in the circulation and especially to the increased cardiac output and not a result of the action of digitalis upon the peripheral vascular system. In normal patients or in those with isolated left ventricular failure, the systemic venous pressure is not elevated and digitalis has no significant effect on it.

Circulatory volume is changed by the cardiac glycosides. For reasons not fully understood, congestive heart failure is accompanied by an increase in the circulating blood volume. Digitalis and related compounds act to decrease the blood volume and probably do so by restoring cardiac compensation and removing the causes underlying the original increase. In patients with normal hearts, however, digitalis may also cause a diminution in circulatory blood volume. The mechanism of this action is still unknown.

Blood pressure is affected in no uniform manner by the cardiac glycosides, but it is lowered, raised or not changed, as one might predict if one assumes that these glycosides act directly on the myocardium to cause a reversion toward normal. For example therapeutic amounts of digitalis cause no constant or significant change in the blood pressure of normal human beings. In patients with heart failure, the administration of digitalis causes variable changes in blood pressure. As one might expect, the pulse pressure may be increased due to a lowering of diastolic pressure. This lowering may be secondary to a reduction of vasomotor tone elevated by a relative anoxia. The systolic pressure may also fall somewhat, especially if its level was high as a result of over-compensation subsequent to the failure. Low systolic pressures due to decompensation are elevated toward normal as digitalis improves cardiac function. It seems clear, therefore, that digitalis affects blood pressure only through its action on the heart and not by any significant effect on the blood vessels or vasomotor center. The

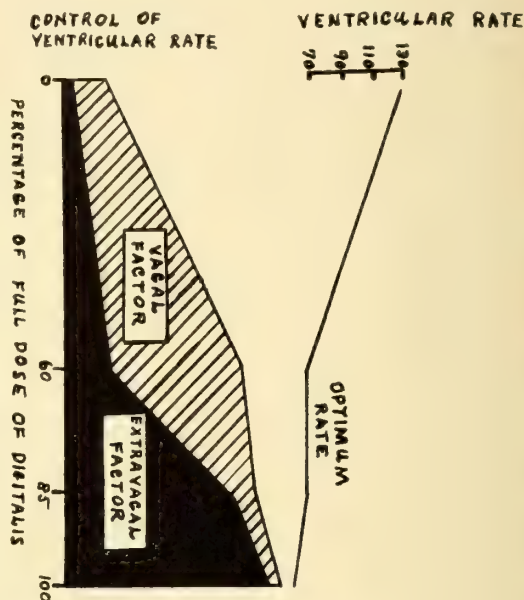
former hesitancy regarding the use of digitalis in hypertensive patients does not appear to have any basis in fact. From the foregoing it would seem that patients who have hypertension and isolated left ventricular failure may be greatly benefited by digitalis.

The mechanical efficiency of the heart muscle appears to be increased by digitalis. Animal experiments indicate that after digitalis the heart is able to do a given amount of work with less consumption of oxygen (Gremels, 1933; Peters and Visscher, 1936). This may be related to the fact that digitalis decreases the diastolic size of the heart, and it has been shown that for a given amount of work the oxygen need of the heart increases as the diastolic size of the heart increases.

Digitalis usually slows the heart rate. However, the present conception of the action of digitalis minimizes the importance of cardiac slowing as a factor in the beneficial effect of the glycoside in heart failure. For many years, the overemphasis placed on the slowing of cardiac rate after digitalis obscured the major and direct action of the drug on the myocardium and also the main indication for its use, namely, cardiac decompensation. Congestive heart failure is often relieved in man by clinical doses of digitalis without evidence of cardiac slowing. Furthermore, if slowing does occur, benefit may be observed earlier than any change in rate. Again, when the rate is decreased by digitalis it is mainly in patients who have a tachycardia accompanying the heart failure. Even in auricular fibrillation where digitalis exerts its most prominent slowing of ventricular rate, the drug usually does not slow the ventricle unless heart failure exists. From these basic clinical observations it is pretty conclusive that digitalis may cause marked improvement in heart failure without intervention of primary cardiac slowing. This conclusion is strengthened by the fact that changes in heart rate are insignificant and variable when full doses of digitalis are given to persons without cardiac failure. The question now remains as to how digitalis brings about ventricular slowing. From early animal experiments and from later work by Gold and co-workers on patients, there appears to be two mechanisms at work. The first mechanism seems to be through the vagus reflexly by way of the carotid sinus and aortic body. From our present knowledge of physiologi-

ogy and in view of the above clinical observations we may assume that the chain of events proceeds in this manner; the heart muscle begins working more efficiently, the cardiac output is increased, more oxygenated blood is present in the area of the aortic body and carotid sinus at any given instant, more afferent impulses travel up the vagus to the cardio-regulatory center, there is improved circulation all over the body and therefore less anoxia, afferent impulses reach the cardio-regulatory center from all over the body probably including the higher centers of the brain which are also less anoxic, more impulses travel down the efferent fibers of the vagus, and the heart rate slows. In other words digitalis causes vagal slowing of the rapid heart rates seen in clinical heart failure by restoring cardiac compensation. That the vagus nerve is involved in this mechanism is proved by the fact that this slowing can be abolished by vagotomy, atropine, or exercise. The fact that exercise abolishes this effect is entirely in agreement with the known physiology of the cardio-regulatory center, and is of some importance in the maintenance of patients with auricular fibrillation. In the treatment of these patients it is not uncommon to find digitalis reducing the rate from 140 to 70 when the patient is at rest. When he is up and about, however, he complains of palpitation and breathlessness. Free physical activity raises the rate to uncomfortable peaks when the mechanism of control is vagal. Fortunately for these patients there apparently is a second mechanism by which digitalis slows the heart rate. This mechanism, for lack of complete understanding of its nature; is called the extravagal action of digitalis. According to Gold, the extravagal mechanism comes more and more into control as the full digitalizing dose is approached. This effect is not abolished by vagotomy, atropine, or exercise. Gold found that when slowing was by the extravagal mechanism, patients with auricular fibrillation rarely showed an acceleration of heart rate above 100 after exercises. This extravagal action of digitalis appears to be due to the depressant action of digitalis on the conduction of auricular impulses through the junctional tissue, and also the result of the direct action of the glycoside on the decompensated myocardium to strengthen the force of its contraction which automatically increases the refractory period of the muscle. A schematic representation of how digitalis seems

to slow the ventricular rate in heart failure will be shown (Figure 3).



There are divergent views as to the effect of digitalis on the coronary blood flow. Some workers believe that the coronary vessels are an exception to the statement that toxic doses are necessary to cause vascular constriction, and they report coronary vasoconstriction from therapeutic amounts (Gilbert and Fenn, 1932). This view has its supporters in the clinical field who contend that digitalis in patients with angina pectoris tends to increase the incidence of attacks of pain. However, Essex, Herrick, and Vischer (1938) using the thermostromuhr method to test the mean blood flow through the circumflex branch of the left coronary artery in trained intact dogs concluded that the glycosides of digitalis lanata have no effect on coronary blood flow, and Gold and coworkers (1938), in a careful and extensive study of 120 selected patients with angina pectoris without decompensation, demonstrated that digitalis does not increase or decrease the incidence of anginal attacks and that even large doses rarely, if ever, produce effective constriction of the coronary arteries.

Withering used digitalis in cardiac dropsy and for many years the foxglove was considered a diuretic. I think it is now generally agreed that digitalis is in no sense a true diuretic and its effects on urine flow are due entirely to its action on the heart and circulation. In normal persons or in patients with heart failure without edema, no diuresis is noted after digitalis. In cases with anasarca due to causes other than congestive heart failure, the glycoside likewise causes no increase in urine output. It seems clear, therefore, that mobilization of edema fluid causes the diuresis and not vice versa. The main cause of edema in congestive heart failure appears to be the increase in hydrostatic pressure in the venous ends of capillaries, preventing the normal resorption of extracellular fluid. As heart failure is relieved and venous congestion reduced, the edema fluid is returned to the blood, and with the simultaneous relief of vascular congestion in the kidney and improved renal function it is then excreted. It must be remembered, however, that despite the effect of digitalis in mobilizing edema fluid in congestive heart failure, about one-half of all patients require additional measures to cause diuresis. Whether this is due to the inability of digitalis to restore full cardiac compensation in these patients is unknown.

Within two to four hours after large oral doses of digitalis, definite alterations may appear in the electrocardiogram. The first changes are noted in the S-T segment or in the T wave itself.

The normally upright T wave may become diminished in amplitude, flat or inverted in one or more leads. The S-T interval may also show depression. Either of these changes may occur alone or both may coincide. These changes seem to be due to a direct action of the glycoside on the heart muscle since they are not abolished by atropine. Of importance is the fact that these changes may simulate those resulting from coronary artery disease or recent coronary occlusion. The PIR interval may also be prolonged by digitalis, and significantly this effect appears somewhat later than those mentioned above. The interval is rarely prolonged greater than 0.25 second. If it is greater than this, pre-existing disease of the conduction system may be assumed. The Q-T portion of the tracing is shortened by digitalis and reflects the fact that the drug lessens the duration of ventricular systole. That the T wave changes usually occur before the P-R interval is prolonged indicates again that digitalis acts first and foremost on the heart muscle itself.

The more important features of the foregoing discussion of the cardio-vascular actions of the cardiac glycosides are summarized in the following table (Figure 4).

DOSAGE ABSORPTION, AND EXCRETION OF THE CARDIAC GLYSOSIDES

We have seen from the foregoing discussion of the chemistry of the cardiac glycosides that the active principles of all the preparations are

RESPONSES TO DIGITALIS IN HEALTH AND DISEASE

Effects Of Digitalis On	Patients With Normal Hearts	Patients With Heart Failure
Ventricular Rate	Slight decrease as a rule	Usually decreased if previously rapid
Blood Pressure	No significant change	No uniform or marked effect. May be increased if low, decreased if high
Venous Pressure	No significant change	Decreased if elevated
Cardiac Size	Decreased below normal	Decreased toward normal
Cardiac Output	Decreased	Increased
Velocity of Blood Flow	Increased or decreased	Increased usually
Circulating Blood Volume	Diminished	Diminished
Symptoms	May have lassitude, dyspnea, substernal pain, etc.	Relief of dyspnea, cyanosis, edema, ascites, etc.

FIGURE 4

Preparation	Oral Maintenance Dose	Digitalizing Dose		Absorption of Oral Dose	Oral Toxic Dose	Latent Period	Duration
		Intravenous	Oral				
Digitalis Leaf	0.1-0.2 GM.	0.3-0.4 GM.	1.5-2 GM.	20%	1.8-3 GM.	4-6 Hours	2-3 Weeks
Digitoxin	.05-0.3 MG.	1.2-2.6 MG.	1.2-2.6 MG.	100%	1.7-5.9 MG.	4-6 Hours	2-3 Weeks
Digoxin	0.25-1 MG.	0.8-2 MG.	2-8 MG.	20-50%	2-12 MG.	1-3 Hours	3.7 Days
Gitalin	0.2-0.8 MG.	2-3 MG.	3.65-8 MG.	40%			10 Days
Lanatoside C	0.25-1.5 MG.	0.8-2 MG.	7.5-20 MG.	10%	6-13 MG.	1-2 Hours	3-8 Days
Lanatosides A, B & C.	0.33-1.33 MG.	0.8-1.7 MG.	4-8.9 MG.	20%	4.3-16.3 MG.	2-3 Hours	3-5 Days
Quabain		0.5-1 MG.				1 Hour	1-2 Days
Scillarens A & B	1-3.2 MG.	0.5-1.7 MG.	8-30 MG.	5-10%	18 MG.		4-5 Days

FIGURE 5

very similar chemically and also that minor changes in the chemical formula do not seem to cause much if any change in their action on the heart muscle. However, these minor chemical differences together with the particular sugars combined with the different aglycones apparently have a major effect on the absorption and excretion, and therefore the dosage of the different glycosides. At any rate, it is a well known fact that there is marked variation in the therapeutic dosage of the various preparations. The amount to be given depends upon the glycoside used and upon the route of administration. From these facts it is clear that the physician must be entirely familiar with the preparation he uses, in order to obtain maximum benefit without intoxication. In order to save time and space, I will summarize the differences in absorption, excretion, and dosage of the major preparations now in use in the following table (Figure 5). From this table it can be seen, first, that roughly 1000 times as much digitalis leaf is required to adequately digitalize a patient as is required of the purified glycosides. Since the three active glycosides contained in digitalis leaf are digitoxin, gitoxin, and gitalin, it is evident that the powdered leaf contains much inert matter. Also only 20% of the oral dose is

absorbed. This might be predicted since digitoxin is the only known glycoside that is completely absorbed by the gastrointestinal tract. From these facts we may draw our conclusions regarding the use of our oldest digitalis preparation. There are two outstanding disadvantages. First, digitalis leaf is an impure preparation containing several different chemical compounds, the quantities of which may vary in different crops of the foxglove plant. Therefore the potency of each batch must be checked against a standard powder. Since there are several methods of standardization, one must be thoroughly familiar with the method used for the preparation he prescribes. The second disadvantage of powdered digitalis is the relatively large dose necessary to secure therapeutic benefit, thus increasing the possibility of gastrointestinal irritation. Digitalis leaf does, however, have some advantages. In the first place it is cheaper, and secondly, since it is a relatively dilute preparation, there is a greater margin of safety. For this same reason it is easier to maintain patients without toxic effects. Stewart finds that many physicians after using digitoxin for a while are shifting back to the whole leaf because they have encountered toxicity in certain patients on maintenance doses of digitoxin. He

further states that when intoxication occurs with the whole leaf it passes quickly and it may only be necessary to reduce the dose, or at most to omit the drug for a day or two. On the other hand the pure glycosides have certain advantages: (1) The glycosides can be given in small doses (milligrams); (2) local gastric irritation, while not often seen with powdered leaf unless several tablets are given at once, is practically non-existent with the glycosides; (3) the glycosides can be prescribed by weight and not by biological units because they are of constant chemical composition; and (4) a particular glycoside can be chosen for an individual problem in therapy. An example of this last advantage is the use of a pure glycoside with a short latent period, such as lanatoside C for rapid intravenous digitalization. Since the cardiac glycosides are pure, highly potent, chemical compounds, our present difficulties in their use stem from inadequate knowledge as to the correct amount required to produce the desired therapeutic results. Most of the recent work indicates, for example, that the initial digitalizing dose of digitoxin has been too low, while the maintenance dose too high; thus the increased incidence of digitalis intoxication when the drug is given over a long period of time. Articles by Stewart, DeGray, and others in 1950 place the average digitalizing dose of digitoxin at 1.6 to 2.2 milligrams as compared to the old idea of 1.2 milligrams. They also find that the maintenance dose of 0.2 milligrams is too high usually, and that it is more nearly in the neighborhood of 0.1 milligrams. Finally, in prescribing any of these drugs, we must remember that patients vary in their tolerance to all of the cardiac glycosides. Therefore if we are to use any of these drugs skillfully we must be thoroughly familiar with the therapeutic responses to be expected and the toxic effects that may be encountered. The final assay of the proper dose is on the individual patient.

DIGITALIS INTOXICATION

The toxic effects of digitalis are largely extensions of the therapeutic actions of the drug. A preparation which will not cause digitalis poisoning when given in excess is also one which will not exert any therapeutic effect. I think this is an important point to remember when we are appraising the claims made by pharmaceutical firms for their particular brands of digitalis, its purified fractions or substitutes.

Withering wrote, "The foxglove when given in very large and quickly repeated doses, occasions sickness, vomiting, purging, giddiness, confused vision, objects appearing green or yellow; increased secretion of urine, with frequent motions to part with it; slow pulse, even as low as 35 in a minute, cold sweats, convulsions, syncope, death — — — . I am doubtful whether it does not sometimes excite a copious flow of saliva."

This description applied to the effects of large acute doses because Withering was unacquainted with prolonged use of maintenance amounts of foxglove. Digitalis poisoning, as we usually see it today, is due to the continued ingestion of the drug in amounts greater than are destroyed or eliminated. The effects noted are gastrointestinal, cardiac, and cerebral.

The gastro-intestinal symptoms of anorexia, nausea and vomiting are among the earliest evidences of digitalis overdosage. Anorexia usually occurs a day or more before nausea and vomiting develop. Nausea next develops and may appear in recurring "waves". Vomiting then occurs but at times it may develop without preliminary anorexia or nausea. Nausea and vomiting may be transitory or entirely absent, and they may also be present even before digitalis as a result of the congestive failure. The fact that they are present before digitalis is given is no contraindication to the use of digitalis. Diarrhea may also be noted and rarely it may be the only gastro-intestinal manifestation of digitalis overdosage. The mechanism of the gastro-intestinal symptoms caused by cardiac glycosides has been the subject of considerable investigation. The bulk of clinical and experimental evidence points to the fact that vomiting is reflex in origin and arises neither from irritation of the alimentary tract nor from direct stimulation of the medulla. The exact site of origin of the afferent stimuli in man is still unknown.

The cardiac effects of digitalis overdosage may cause alterations in cardiac rate and rhythm simulating almost every known type of arrhythmia seen clinically. Probably the most frequent cardiac effect of digitalis poisoning is the occurrence of extrasystoles. These usually originate in the ventricle but can arise from the auricle. The cause of the ectopic beats is the increased irritability of the myocardium produced by excessive amounts of digitalis. If the extrasystoles are frequent, the ventricular rate in-

creases and over-shadows a primary slowing. However, the toxic effect on the A-V conduction system may be the major one to cause extreme slowing of the heart. The usually accepted rule is to stop digitalis if the ventricular rate falls to 60 beats per minute or below. Toxic amounts of the cardiac glycosides may also cause sufficient prolongation of the A-V conduction to produce dropped beats and at times complete auriculoventricular dissociation. Sinus arrhythmia occurs as an early and minor toxic effect of digitalis and since it can be abolished by atropine it is probably vagal in origin. Paroxysmal tachycardia may arise either from the ventricle or auricle and call for discontinuance of the drug. Auricular fibrillation can be caused by large doses of digitalis. The occurrence of this arrhythmia usually calls for the temporary discontinuance of the drug. That digitalis overdosage can cause fibrillation of the auricles is not a contraindication to the use of the drug in that condition. Ventricular fibrillation is probably the commonest cause of death from digitalis poisoning. It is preceded by ventricular extrasystoles.

Among the common cerebral effects of digitalis are headache, fatigue, malaise, and drowsiness. Mental symptoms include disorientation, confusion, aphasia, and even delirium and hallucinations. Convulsions have been known to occur. These effects are particularly prone to develop in elderly arteriosclerotic patients and the exact role played by digitalis is uncertain. Vision is often blurred. White borders or halos may appear on dark objects ("white vision"). Color vision may be disturbed and objects appear yellow and green, or less frequently blue and red. Transitory amblyopia, diplopia and scotomata may also occur. An explanation for these cerebral effects of the cardiac glycosides is not available.

INDICATIONS AND CONTRAINDICATIONS

The indications for digitalis are sharply defined. It is a potent drug and should be given only when indicated. When given to the normal subject it decreases the cardiac output as much as 30% and decreases the size of the heart. The subject may suffer angina on effort because of the decline in cardiac output. The indications for digitalis are in the main two (1) congestive heart failure, either in the acute stage, such as in pulmonary edema, or in the more chronic forms, and (2) certain irregularities of the heart rhythm.

Some special aspects of congestive heart failure where digitalis may be used are acute myocarditis when heart failure occurs. In active rheumatic carditis it must be used carefully in order not to precipitate toxic manifestations.

It may be used in myocardial infarction when heart failure occurs early or late. About the end of the first week or ten days the possibility of rupture because of more vigorous action of the heart must be kept in mind.

It is used in ventricular paroxysmal tachycardia only when quinidine will not stop an attack and heart failure occurs.

It is used in the presence of congestive heart failure due to hyperthyroidism whether auricular fibrillation or normal rhythm is present. More than the usual amounts may be required to reduce the ventricular rate when auricular fibrillation prevails. Digitalis should be continued in auricular fibrillation until after propylthiouracil and or thyroidectomy have provided an opportunity for spontaneous reversion to normal rhythm before quinidine is tried. It is used if auricular flutter is present.

Christian suggests the use of digitalis in organic heart disease before the onset of failure in order to prevent or delay the onset of failure. The drug has not been used to any great extent for this purpose because it is difficult to prove that benefit results.

With regard to rhythm irregularities, it may be used to stop auricular premature contractions when they give rise to symptoms. It may be tried if other measures, such as sedatives, have not been effective.

In auricular fibrillation it has the following uses:

1. It is employed to slow the ventricular rate.
2. It may cause reversion to normal sinus rhythm, but there is no evidence that digitalis "fixes" this rhythm.

3. It may prevent recurrences of paroxysmal auricular fibrillation in some patients who are not benefited by quinidine.

It is usually the drug of first choice in the treatment of auricular flutter. It first increases the degree of auriculoventricular block and then causes reversion to normal rhythm. There may be a transit phase of auricular fibrillation. More than the usual therapeutic amount may be required before reversion to normal rhythm occurs.

Digitalis may be used when there is failure in the presence of complete heart block or incom-

plete heart block if the block is not due to digitalis.

Stewart believes that the cardiac glycosides are the drugs of first choice in treating the supraventricular paroxysmal tachycardias, such as auricular paroxysmal tachycardia and auriculoventricular paroxysmal tachycardia. He recommends 0.1 gm. to 0.3 gm. of the powdered leaf to terminate supraventricular paroxysmal tachycardia or auricular flutter in very young infants. Rapid digitalization with lanatoside C has been recently recommended in the treatment of these rhythms in adults; 0.8 mg. may be given intravenously. If there is no response in thirty minutes to one hour, another 0.8 mg. is injected intravenously. In other instances, 1.6 mgm. may be given in one dose.

Digitalis is contraindicated in the presence of ventricular paroxysmal tachycardia, unless heart failure occurs and quinidine will not terminate the attack.

It is contraindicated if ventricular premature contractions are frequent, but if the premature beats are due to congestive heart failure they may disappear upon digitalization. However, on the other hand, ventricular premature contractions may be increased in number by digitalis and ventricular paroxysmal tachycardia may be precipitated.

The cardiac glycosides are contraindicated in the presence of chronic constrictive pericarditis unless auricular fibrillation is present, in which case it is used to keep the ventricular rate slow.

They are contraindicated in the presence of hypersensitivity of carotid sinuses, as they may precipitate attacks because of their vagal effects. If heart failure is present and a digitalis preparation is required, the drug may be used and atropine given at the same time in order to prevent attacks.

Digitalis is contraindicated in the presence of transient complete heart block with Adams-Stokes attacks, because it may induce attacks and slow the ventricular rate further.

Calcium salts should not be used intravenously when the patient is digitalized, as death has been reported from its synergistic action with digitalis. In animals, ventricular premature contractions are more easily induced when digitalis and calcium are given at the same time than when either one is given alone.

Ventricular paroxysmal tachycardia and ventricular fibrillation have been reported as re-

sulting from the use of quinidine and digitalis simultaneously. It seems safer when quinidine is to be used in the treatment of auricular fibrillation, to first retard the ventricular rate with digitalis which is then discontinued after which quinidine is given. This same plan may be followed in the treatment of auricular flutter if digitalis does not cause reversion.

There are a few papers dealing with the combined use of digitalis and large amounts of quinidine in the treatment of chronic auricular fibrillation and supraventricular paroxysmal tachycardia. The general opinion appears to be that extreme care should be exercised in this procedure.

Digitalis is generally believed to be without benefit in the treatment of angina pectoris and therefore should not be used unless heart failure is present.

SUMMARY

1. The cardiac glycosides have a specific and powerful action on the myocardium which is unrivaled in the treatment of heart failure.

2. These drugs are all closely related chemically and appear to vary little if any in their action on the heart.

3. The active chemical compounds are aglycones or genins which when combined with certain sugars form the pure glycosides.

4. The particular sugars with which the aglycones are combined seem to have a marked effect upon the gastro-intestinal and myocardial absorption of the glycosides, thus causing a wide variation in their therapeutic dosages.

5. The general consensus of opinion is that the primary site of action of these drugs is on the heart muscle.

6. The mechanism of this action is to shorten the muscle fibers and cause the heart muscle to contract more forcefully.

7. Digitalis brings about cardiac slowing by two major mechanisms; vagal and extravagal.

8. The mechanical efficiency of the heart is apparently increased by the cardiac glycosides for the heart is able to do more work per unit of oxygen used.

9. The diuretic effect of the cardiac glycosides is secondary to improved cardiac function.

10. There is marked variation in the dosage, absorption, and excretion of the different cardiac glycosides, and there is also a rather wide variation in the tolerance of different patients to these drugs. It therefore is mandatory that the

physician know the drug he is using, the therapeutic responses to be expected, and the toxic effects that may be encountered.

11. The indications for the cardiac glycosides are sharply defined and they should not be used indiscriminately because they lower the cardiac output and may cause anginal pain in patients with normal hearts.

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.

2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)

3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.

4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.

5. Submit manuscript typewritten and double-spaced.

6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

Editorial

ANNUAL MEETING AMERICAN MEDICAL ASSOCIATION ATLANTIC CITY — NEW JERSEY

The Conference of Presidents and other Officers of State Medical Associations convened in Atlantic City, N. J., Sunday, June 10, 1951, at 2:00 P.M., Julian P. Price, M.D. of Florence, South Carolina, presiding. Attendance was in excess of 500, including many members of the

House of Delegates and, with an excellent program, possibly will be recorded as the most outstanding of its sessions thus far.

W. Andrew Bunten, M.D., of Cheyenne, Wyoming, Past President of the Wyoming State Medical Society and President-Elect of this Conference presented the subject: "A Physician Views Medicine". He reviewed the history of medicine and its service to mankind; the progress and achievements in combating disease; portrayed the physician's role as family counselor; the growth of voluntary health insurance plans; and emphasized the need for the physician to assume his rightful place and leadership in civic programs and if need be, seek legislator membership. He stated: "No one possesses a more intimate knowledge of the American Way of Life than does the physician. Properly applied, along with his training and ability, could lend itself immeasurably in moulding our future course."

Edwin F. Abels of Lawrence, Kansas, Past President of the National Editorial Association and Editor of The Lawrence Outlook, addressed the gathering on how "An Editor Views Medicine". Pointing out that the local small press represents and speaks to the large majority of Americans from the home town, with the threat also leveled at the public free press, expressed the sincerity of the local publishers in welcoming the example set by the great American Medical Association in speaking the truth and endeavoring to arouse public apathy to the dangers which lie ahead in the blind pursuit of a socialized economy.

The Most Reverend John J. Wright, D.D., Ph.D., Roman Catholic Bishop of the Diocese of Worcester, Massachusetts, delivered a stirring address on how "A Clergyman Views Medicine". The peoples of the World must first become morally right, honest and speak the simple truths before there will be hope for peace to come, he stated. Man has so completely discarded these basic virtues that there is little wonder chaos is so rampant today and the future so dismal, replete in distrust, discontentment and loss of faith.

Honorable Richard M. Nixon, of Whittier, California, United States Senator from the State of California, set forth his opinion on how "A Legislator views Medicine". Recognizing that the medical profession represents the highest level of education in our Country, he expressed

the belief that the physician should give freely of his wisdom to guide legislators on all national issues. He told the doctors that they owe it to themselves and to the Nation to stay in politics.

Monday evening, June eleventh, at Hotel Traymore, was the scene of a dinner-meeting given by the Medical Society of New Jersey to Officers and Members of the House of Delegates of AMA, on which occasion Dave Beck, Executive Vice-President of the International Brotherhood of Teamsters, American Federation of Labor, declared that the road to final solution to bring adequate medical care within the economic grasp of our citizens is not through socializing the medical profession. The answer as proposed by advocates of Government-controlled medicine is contrary to our economic structure and goes beyond our traditional guarantees. Any system which proposes such modifications in our way of living and doing things would lead to a dangerous socialistic trend and cannot be tolerated. Such a system would destroy our liberty. To the medical profession, he continued: "You have earned the respect of your fellow country-men over and over through the work you have done on Main Street, in our great cities, on the battlefield, in our hospitals and in the classrooms. The answer lies in Voluntary medical programs—prepaid medical plans. This system of Voluntary health care is making a great record in this Country. Let us continue the Voluntary way of doing things in America—it is our best protection against any compulsory way. It is compulsion and interference with our individual freedom and initiative which lead to State control—dictatorship, Fascism, Communism. We will not permit any of these to take root in the profession of medicine."

Introduced by Louis H. Bauer, M.D., Chairman of the Board of Trustees and President-elect of the American Medical Association, on Tuesday evening in the Ball Room of Atlantic City Auditorium, John W. Cline, President of AMA, declared that: "No health crisis or medical emergency exists in this Country" and warned that the real danger lies in the double threat of war abroad and loss of freedom at home. In his inaugural address, broadcast nationwide during ceremonies at the 100th annual session of AMA, he expressed "deep and abiding faith in the intelligence and integrity of the American people," adding that "they will respond as they did when their medical welfare and their medi-

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cal freedom were threatened." Calling for constant vigilance, American doctors will continue to "oppose socialistic schemes which would jeopardize the freedom of any segment of our society." "American medicine could not have attained its present position without the assistance and cooperation of our educational institutions, our scientists, our colleagues in public health, our hospitals, nurses, dentists, labor and management, and all the American people—working with initiative and independence toward the same goal. Together we have made great progress in the fight against death and disease, until today we are the healthiest large nation in the world.

Dr. David B. Allman of Atlantic City was selected to fill out Dr. Bauer's unexpired term (1954) on the Board of Trustees and Dr. Walter B. Martin of Norfolk, Virginia, was reelected to a five-year term on the Board.

Dr. Oscar B. Hunter of Washington, D. C., was unanimously chosen AMA vice-president.

Other officers re-elected were: Dr. George F. Lull, Chicago, secretary; Dr. J. J. Moore, Chicago, treasurer; Dr. F. F. Borzell, Philadelphia, speaker of the House of Delegates; and Dr. James R. Reuling, Bayside, N. Y., vice-speaker.

The AMA Coordinating Committee, in charge of the National Education Campaign since its inception in January, 1949, will continue to function, again headed by Dr. Elmer L. Henderson, Louisville, Ky., retiring president of AMA. The Board of Trustees announced that the public relations firm of Whitaker and Baxter would be retained for another year.

At the close of registration Thursday, June fourteenth, 11,987 physicians had registered for the 100th Annual Session of AMA. Among the membership from Arizona were registered: Drs. Charles L. von Pohle, Chandler; V. E. Frazier, Mesa; Joseph Bank, Frederick W. Coleman, George S. Enfield, Robert S. Flinn, Jesse D. Hamer (Delegate), Charles Kalil, Phil H. Lovelless, H. J. McKeown, Wallace M. Meyer, Robert A. Price, Maurice R. Richter and James M. Whitelaw, all of Phoenix; and Benson Bloom, O. J. Farness, Walter T. Hileman, Donald F. Hill, W. Paul Holbrook, Arnold L. Lieberman, Teresa McGovern, Joy Alba Omer, Raymond F. Oyler, Jackman Pyre, John J. Rupp, Delbert L. Secrist, Henry J. Stanford, Alden B. Thompson, Hugh C. Thompson, William Kirby West, and Marguerite S. Williams, all of Tucson.

PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL M. G. H. CASE NO. 29341

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

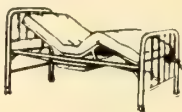
A thirty-six-year-old white bank clerk entered the hospital because of increasing dyspnea of three months duration.

The patient had had a long history of respiratory distress. Nineteen years prior to admission, while in college, he had had two attacks of pneumonia within a few months. Tuberculosis was suspected but chest plates failed to confirm the diagnosis. For the next ten or twelve years he was well except for more than the usual number of colds. Seven years before entry he was examined for life insurance; in view of his past history an x-ray film of the chest was taken which showed a lung tumor. He was admitted to an outside hospital where, following artificial pneumothorax, an exploratory thoracotomy was performed. A diagnosis of inoperable malignant tumor of the lung was made. He recovered from the operation and returned to work, free of symptoms.

During the next two years he lost about three months every year from his work because of upper respiratory infections. He was given x-ray treatment every three months. Two years later, that is, three years prior to admission, he had pneumonia again. About one year prior to admission he was told by his physicians that they had considered his lung tumor malignant and incurable but that he had lived for so many years they had become convinced that the tumor was benign. For the next two or three months he developed episodes of palpitation which he believed were due to "nerves". These passed off and did not return. Three months prior to admission he had the grippe. Following this there was a gradual onset of dyspnea, which prevented him from walking up hill or climbing stairs. Three weeks before entry the dyspnea cleared up for a short time, but soon returned and became progressively worse. There was no history of tuberculosis.



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Physical examination showed a thin, pale man with a sallow complexion. There was some increased prominence of the veins of the forehead and neck. The left border of cardiac dullness was 16 cm. to the left of the midline in the seventh interspace. The heart was otherwise normal. The lungs showed dullness over the right apex, becoming flat at about the level of the fourth rib. The entire right lower lung was flat, with absent breath sounds and decreased fremitus. The left lung was resonant, but there were occasional rales at the base. The abdomen was negative except for a tender liver edge, which could be percussed 8 cm. below the costal margin.

The blood pressure was 110 systolic, 90 diastolic. The pulse rate was between 100 and 130, and the respiration between 20 and 25. The temperature was normal.

The hemoglobin was 11.3 gm per 100 c.c., and the white-cell count 13,600. A blood Hinton test was negative. Two sputum examinations were negative for tubercle bacilli.

An x-ray film of the chest showed complete obscuring of the lower two thirds of the right lung field by fluid. The right upper lung showed increased density with honeycombing. A grid film showed the right main bronchus visible for about 2 cm., beyond which it could not be made out. The left lung field was clear. The heart shadow was tremendous, and the configuration suggested pericardial effusion. Fluoroscopically no pulsation was demonstrable. The mediastinum was not displaced. Repeated x-ray examinations revealed no additional findings. A chest tap in the eighth space in the subscapular region yielded 30 c.c. of light-amber fluid, followed by 220 c.c. of what appeared to be whole blood. This was removed from several directions and depths. A repeat tap in the seventh space in the midaxilla again yielded 30 c.c. of blood. No tumor cells were seen in the fluid, which contained innumerable red cells. Two days later the venous pressure was recorded at 330 mm. of water (normal control, 137 mm.) The patient was refluoroscoped at that time. A definite pulsation of the heart could be seen. No change in the contour of the heart could be demonstrated on changing the position of the patient from erect to horizontal. The left border of the heart shadow was convex and without any break in the smooth curve to indicate the limits of the pulmonary conus and left ventricle. Lam-

inography showed the right main bronchus to end sharply 2 cm. from its bifurcation. No air could be seen entering the lower and middle lobes. There was narrowing of the upper bronchus extending into the areated portion of the lung. Several small air-filled areas were seen in the region of the lower lobe. A dense soft-tissue mass was seen lying between these and the blocked right main bronchus. The outline of the mass could not be clearly defined. An electrocardiogram was interpreted as showing sinus tachycardia, with a rate of 120, slight right-axis deviation, low T_1 , total inversion of CF_2 and a very low T in CF_4 and CF_5 .

The patient's dyspnea increased progressively. He died on the twelfth hospital day.

DR. W. W. WATKINS

The first impression left after reading over this case record is that Judge Woodman has missed the calling for which he seems to have a peculiar genius,—namely that of thimble-rigger at a county fair. If he could have in front of him three little shells or thimbles and a small rubber ball, usually called a "pea", and should deftly manipulate these and then offer to bet the yokel, now portrayed by me, that he cannot tell under which shell or thimble the "pea" is located, the situation would exactly simulate that in which we now find ourselves. The "pea" is the diagnosis, the three shells or thimbles are (1) benign lung tumor, (2) malignant lung tumor, and (3) inflammatory lesion. The thimble-rigging or three shell game is represented by what we are told about this lesion, which was diagnosed, undiagnosed, misdiagnosed, and finally wound up by killing the patient.

While getting Dr. Woodman's vocational aptitudes correctly diagnosed, I would like to pause a moment and turn the heavy artillery on the physician who undiagnosed the case because the patient persisted in living. This patient had been given treatment by a hard-working radiologist, who irradiated the lung lesion every three months over a period of two years. Yet this physician, with a scurrilous skepticism about the efficacy of x-ray treatments, would change his own diagnosis before he would give the radiologist credit for slowing down the progress of this inoperable malignancy.

But let's get back to the hopeless task of guessing under which shell the "pea" is hidden, with the odds well in favor of Dr. Woodman's

having palmed it and each thimble or shell being empty.

The whole question would seem to hinge on whether the chest surgeon who opened this chest seven years back was wrong in his diagnosis of an inoperable malignant lesion, when he looked in and probably palpated the tissues. A lung tumor had been shown by x-ray so we will consider the possibility of the "pea" being under the thimble of BENIGN TUMOR, misdiagnosed by the surgeon at the time of the thoractomy, as being malignant and inoperable. We are not told whether this conclusion was based on the appearance or feel of the tumor, or on tissue examination. It should have been based on all three, but it would be misfeasance, malfeasance and nonfeasance for a judge to withhold a tissue report, if such examination was made. So, we assume none was made, and assign these grave offenses to the surgeon, rather than the judge. The appearance and feel of a lung lesion cannot be accepted as conclusive in making a diagnosis of the nature of a lung tumor or other lung lesion. The pathologist must decide the question. The benign adenoma can be associated with atelectasis and inflammatory reaction which might closely simulate an infiltrating malignancy. We know this patient did have recurrent lung infections, so we would expect extensive fibrotic changes in the lung tissues very deceptive to palpation. This man was only 29 years of age when the tumor was discovered; this is a little young for lung cancer because he has not yet had time to subject his bronchi and lung tissue to the necessary 20 to 25 years exposure to cigarette smoke and its carcinogenic phenanthrenes. Finally, we would not trust the surgical judgment of a chest surgeon who would nonchalantly make a diagnosis of inoperable cancer of the lungs in a 29 year

Well, how about the CANCER thimble? Maybe claim the "pea" should be under the benign tumor thimble. We lift the shell and the "pea" is not there!

Well,—how about the cancer thimble? Maybe the chest surgeon was right the first time, until the radiologist misled him by keeping the patient alive too long. In the terminal stages the lesion does take on the aspects of an extending malignancy. We now have more x-ray findings than we know what to do with,—yet we could use more. There is pleural fluid; there is pericardial fluid; a visible mass of soft tissue density is in

right lower thorax, and this appears to be obstructing the main right bronchus. Even with a blocked bronchus there was no mediastinal shift, which would seem to exclude gross atelectasis, and indicate that the right side density is fluid, consolidation, or tumor or a combination of these. We could stand to know whether the soft tissue mass found in the later stages was at the same locality as the tumor shadow shown seven years back. We do not know this, and since the point is a vital one and must have been known to the observers of this patient, and, therefore, should be available to us, we can only conclude that withholding this information is a part of the legerdemain of thimble-rigging. If we want to bet on malignancy, we have quite a little support. A lung tumor demonstrated by x-ray, after a long history of recurrent lung infections. A thoracotomy confirmed the tumor, interpreted as a malignant one and inoperable. In further support, the following quotation is offered, from an article by Dotter, Steinberg and Holman, in the Amer. Jour. of Roent., of August, 1950: "Exploratory thoracotomy is now proved to be a safe and satisfactory method for establishing *with certainly* the nature and extent of pulmonary neoplasms." It is true these writers anticipate that tissue will be obtained and the certainty of the diagnosis will be furnished by the pathologist,—a link which is missing in our case. It is also true that this patient's obstinacy in living too long made the physician change his mind about the character of the lesion. But we have already suggested that this vacillation in diagnosis was based on an incredible and scurrilous absence of faith in the efficacy of the x-ray treatments, which this man seems to have had in abundance. So, we indicate the thimble of MALIGNANT TUMOR. We lift the thimble, and what do we see? You are right,—no "pea!"

Thimble-rigger Woodman says we can still win, if we locate the "pea" under the third shell, and give it a name.

Was the original tumor benign and all subsequent developments due to infections one after the other, with these infections finally involving the pleura, pericardium and heart to a fatal degree?

Was the tumor benign and did the repeated x-ray treatments induce a radiation fibrosis and subsequent infection? We know nothing about the amount of radiation given, but if it was aimed

at slowing down a malignant process, which must have been the case since this was the diagnosis at that time, the patient must have received from 1000 r to 2500 r every three months for two years, as stated. This could build up to quite a tissue dose.

Was the tumor benign in the outset, with a malignant metamorphosis in the later stages? Adenomas of the lung are capable of doing this, and the main reason for removing them whenever discovered and diagnosed, is to avoid this development.

Was the original tumor a benign one and did a second tumor of malignant type develop *de novo* in the same lung? Such cases are recorded, and this is just about the sort of stunt our jocular judges would pull on us.

Was the original lesion and all subsequent developments due to infection,—without any tumor at all? That would be too much. We are approaching the Christmas season, when good will, brotherly love and other Christian virtues should prevail, and I do not think our judges, who have shown an almost unimaginable capacity for dishing out punishment,—would sink so low as this,—at Christmas.

Having buttressed myself with an alibi in every imaginable direction, I am now prepared to lift the third shell,—and to find the “pea” not there, but secreted in thimble-rigger Woodman’s palm—the logical and ethical technic whenever any respectable practitioner of thimble-riggering deals with a susceptible yokel. I am betting in this order of probability:—

Shell No. 1. Bronchogenic carcinoma, whose progress was slowed up by radiotherapy, but which eventually spread into a fatal dissemination.

Shell No. 2. Original tumor benign, but with a malignant metamorphosis in the later stages.

Shell No. 3. Original tumor benign, with a super-added separate malignant growth.

4. The “pea” in Woodman’s palm. Benign tumor, with tissue changes and all subsequent developments due to infection.

DIFFERENTIAL DIAGNOSIS

Dr. C. Sidney Burwell*: I should like to try to reconstruct some stages of this gentleman’s course, beginning at the time he came into the hospital, to see what specific statements we can make that seem reasonably acceptable concern-

ing the anatomic and functional situation of the heart and lungs.

In the first place it seems to me demonstrable that this man had an interference with the entry of blood into his heart—that he had pericardial tamponade. This conclusion is based on the following observations. He had distended neck veins and elevated venous pressure; there is no mention of the development of collateral circulation from either the superior or inferior caval areas. We do not have a measurement of the venous pressure on the femoral vein, but there was evidence on physical examination that the liver was greatly enlarged and tender. I should accept that as evidence that he had an elevated pressure in his whole venous system. To that should be added the observation on his pulse pressure, which was very low,—only 20 mm.,—with a low systolic and a high diastolic pressure. No statement is made about the presence or absence of paradoxical quality. The patient had an extremely rapid heart rate without fever, again a characteristic finding in those who suffer from obstruction of the entry of blood into the right side of the heart. This conviction of the presence of cardiac tamponade is strengthened by the observations that seem to indicate that he had a pericardial effusion of considerable size—namely, a very large heart shadow and what could be described as an “expressionless” heart, which neither moved nor exhibited the landmarks on the contour which we are accustomed to recognize. Thus he had a large, nonpulsating, smooth, heart shadow, combined with evidence of obstruction to the entry of blood into the heart, and I think we can say that he had pericardial effusion, with obstruction to the flow of blood from the venous system into the heart.

Now let us turn our attention to the pulmonary situation at the time he came into the hospital. That also seems to me to be impressive from the point of view of its mechanics rather than from the point of view of information concerning its etiology. The patient had, quite clearly, a long history of progressive obstruction to the bronchi of the right lung. I surmise that the course of events was an obstruction to one or the other branch of the right bronchus, leading to atelectasis beyond the point of obstruction and to the development of bronchiectatic cavitation, probably recurrent infections in the atelectatic lung, destruction of lung tissue

*Research professor of clinical medicine and Dean, Harvard Medical School.

and the leaving of this honey-combed structure as the late result of bronchial obstruction. It seems to me that that meets the situation better than the possibility—the remote possibility it seems to me—of congenital polycystic disease of the lung. This man, I should say, had had a series of collapses of the middle and right lower lobes, ending up in the situation in which he entered the Hospital. More recently he had probably had beginning obstruction of the upper branch of the right main bronchus, with a similar change in the right upper lobe. This I should place pericardial effusion and pericardial tamponade as the first part of our diagnosis, and bronchial obstruction with atelectasis and bronchiectasis as the second.

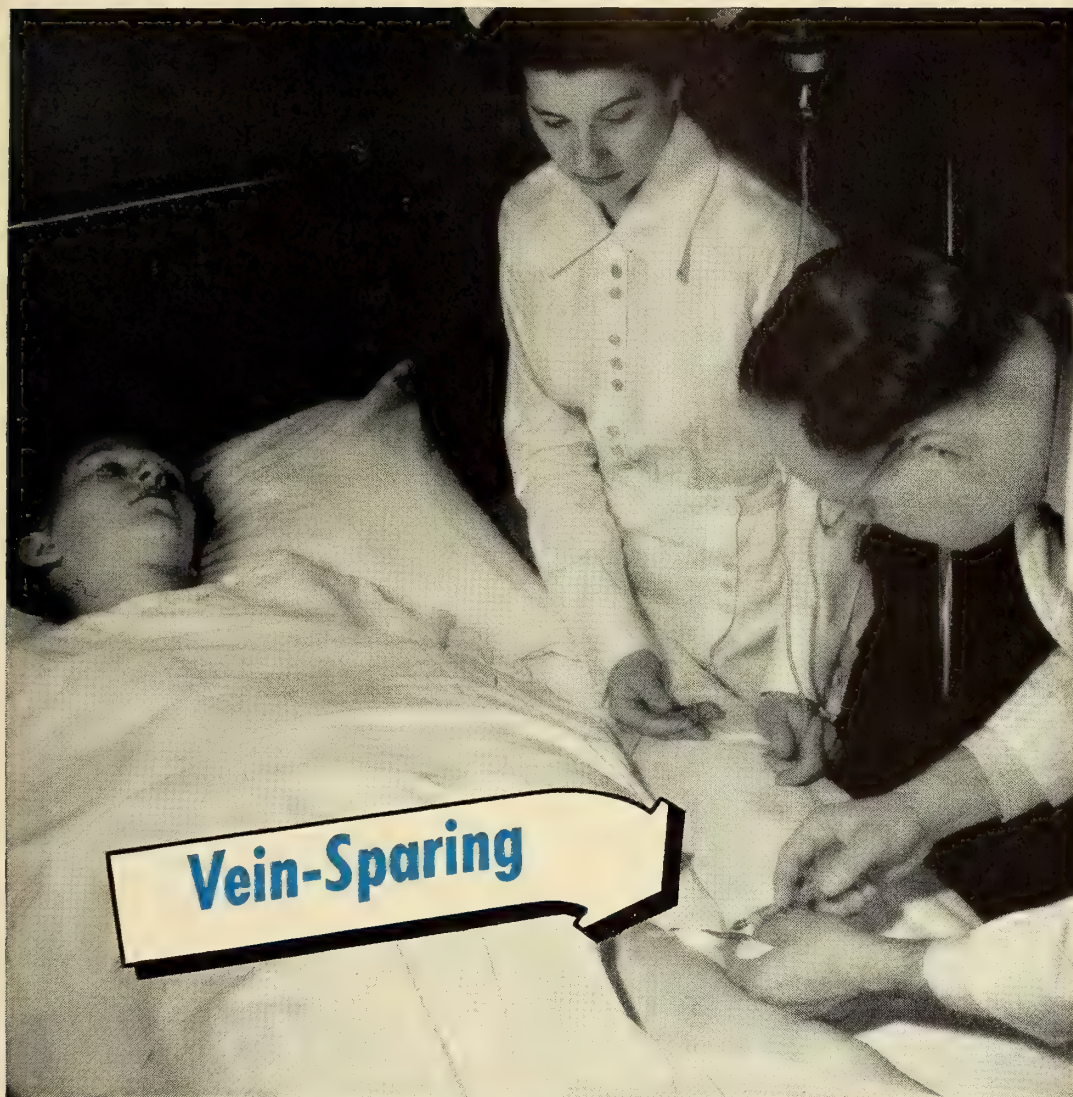
Then we come to the most important and difficult part of the discussion—the basis for these mechanical changes in the lung and heart. Are they to be placed fundamentally on an inflammatory disease or on a neoplastic basis? Let us consider the possibility of a unitarian basis—that everything can be explained by one etiologic factor. What about tuberculosis? We know that tuberculosis of the bronchi is commoner than we thought; that enlarged lymph nodes in the mediastinum or the hilus of the lung may invade the bronchi and lead to inflammatory stricture and to obstruction. Let us consider the possibility that he had reactivation of the mediastinal nodes and invasion of the pericardium by tuberculosis. It seems to me there are at least three very important pieces of evidence against the hypothesis that it had been or was tuberculosis, particularly the latter. One is the fact that he was quite free of fever, and I take it that the observation of a normal temperature was not a single isolated reading at a moment after a cold bath or something of that sort, but did really reflect the situation while he was in the hospital. I see from the chart that he never had fever over 101°F. and that it was usually around 99. That seems to me strong evidence, not final, against an active pericardial tuberculosis. The second piece of evidence against the possibility of tuberculous pericarditis is the presence of blood in the fluid that was removed presumably from the pleural cavity. It may have been removed from some other cavity in relation to the right lung since the first tap conceivably might have been into the pericardium; but wherever it came from the fluid was so bloody that it was less characteristic

of a tuberculous lesion than of a neoplasm involving either the pleura or the pericardium, or both. There is particular case for the position, so far as I can find out, that a primarily tuberculous lesion may undergo malignant degeneration and be the site of tumor. Another important argument against the presence of tuberculosis is the observation seven years before entry, when his chest was opened and the surgeon, who had the inestimable advantage of a direct view, saw something he believed to be an inoperable malignant tumor of the lung. It is conceivable that that was on a tuberculous basis, but I think that it is much likelier to have been a neoplasm.

If we set aside tuberculosis, we are then confronted with the necessity of postulating a neoplasm. This certainly the commonest cause of bronchial obstruction. Assuming it was a tumor, it had the extraordinary dual capacity of existing at least seven years—possibly more—and at the same time having done something recently that sounds very much like malignant invasion of neighboring structures. We must consider various types of benign tumors that obstruct the bronchus—the adenomas and various other ones, —some of which may undergo malignant degeneration after years of growing. We must consider lymphoma. It does not appear in the record whether or not the x-ray treatment, which was faithfully administered, had any effect. However, if it had had an effect, we probably should have been so informed. I am trying to interpret that evidence, such as it is, as indicating that it was not the type of specific improvement after x-ray that we should expect if we were dealing with a lymphoma.

There is a curious silence about the state of this man's cough and sputum. I think one must interpret that as indicating that cough and sputum were not remarkable, and I derive from that the suggestion that hemoptysis was not a vigorously presenting symptom.

So we have quite an assignment—a neoplasm that obstructed the bronchus but did not produce much cough, did not produce large amounts of sputum, did not lead to hemoptysis and had lasted all these years, to explode in an extension to the pleural and pericardial cavities. At the time of the onset of his disease, this man was twenty-nine years old, a situation that further narrows the probabilities regarding the nature of the hypothetical neoplastic process. I do not



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RESEARCH IN THE SERVICE OF MEDICINE **SEARLE**

WHEN WRITING ADVERTISERS PLEASE MENTION THIS JOURNAL

think, by the way, that he had an aneurysm. There is no suggestion in his history or in the serologic findings. The patient was too youthful to have had an aneurysm that lasted as long as this, and I do not believe that the blood that came out at the time the chest tap was done was due to the entrance of the needle into an aneurysm.

If we ask ourselves what are the types of neoplasm that might fulfill this order, we certainly should have to consider carefully the small group of tumors arising from the mediastinum—the dermoid cyst, the teratoid tumor and so on. These do occur in men of this age. Most of them make themselves known before thirty or forty. Most of them have announced themselves, if they are going to grow, by the time the patient is forty. They almost always start in the anterior mediastinum and are more apt to go to the right than to the left. They are known to compress and occlude the right main bronchus or its main branches, and they may secondarily undergo late in their development the type of malignant change that it seems to me is suggested by the recent developments in this man's history. But, unhappily for me, he never spit up any hair or teeth or had any of the other charming observations that serve to make a positive identification of such a tumor. However, it seems to me that that group—probably a dermoid cyst with malignant change—fits the bill better than any other type of tumor I can think of.

The commonest tumor, of course, to give this kind of termination is bronchiogenic carcinoma. Bronchiogenic carcinoma with an onset at twenty is not impossible, but one that lasts for seven years is certainly an extreme rarity. According to what statistics I could put my fingers on, the great majority of people with bronchiogenic carcinoma do not live for more than five years. In fact the longest duration that I could find in recorded cases of bronchiogenic carcinoma was between five and six years.

There is one other point. This man had had attacks of palpitation. Whether these were because he was nervous, or because he was anemic, or whether these attacks were associated with paroxysms of tachycardia or fibrillation I do not know. Such paroxysms occur frequently in people with pulmonary or mediastinal carcinoma, or with actual invasion of the pericardium by carcinoma, and the record does

suggest that these attacks may have been brought on by such a mechanism.

I shall conclude by saying that I believe this man had a pericardial effusion, pleural effusion and bronchial obstruction with atelectasis, and that this was based on an extramural neoplasm that eventually involved the walls of the bronchi. This tumor was originally benign but eventually underwent malignant change and extended to the pericardium. Of all types of neoplasm, I consider a dermoid cyst to be the likeliest origin.

When one thinks of pericardial obstruction or distention in a case of neoplasm, one has to consider the possibility that it is due not to fluid but to actual invasion of the pericardial cavity by solid tumor. I know only two ways to make the diagnosis: to find cells in the pericardial fluid, which is comforting, or to see a shadow of the pericardium that is not smooth but lumpy. That may be inflammatory, of course, but is likely to be tumor.

Dr. Benjamin Castleman: Dr. Sweet, you said that the pericardium was tapped. Is that correct?

Dr. Richard H. Sweet: Yes. The reason it is not in the record is that I did it myself and forgot to write it down.

I did a pericardial tap through the paraxi-phoid region first and obtained fluid readily. But it looked to me to be whole blood, and after drawing off a few hundred cubic centimeters, I withdrew the needle because I did not want to bleed the man to death. At the suggestion of Dr. Conger Williams, who saw this man with me, I then inserted the needle laterally to the first tap and the same kind of fluid was obtained; I could feel the pulsation of the heart muscle with the needle. We were sure that he had a massive effusion. Since the fluid was so much like whole blood and since the patient had a red-cell count of 2,500,000, I desisted. At a later chest tap we also removed whole blood.

Dr. Burwell: If it was fluid blood, and I think it must have been, that strengthens the case for rapidly growing neoplastic invasion. The presence of blood in the pericardium is due either to trauma, to cardiac rupture or to neoplasm. The inflammatory fluid from tuberculosis may contain red cells, but it is not usually grossly bloody.

What about his sputum?

Dr. Sweet: The patient never had any

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hemoptysis. He had a lot of cough and Dr. Burwell was correct in his interpretation of the bouts of what the doctors called variously grippe, pneumonia or what not, which must have been due to bronchial obstruction. After the patient died I obtained a report from the surgeon who operated on him seven years previously. He was convinced that the pulmonary tumor was a carcinoma.

Dr. Burwell: Not a shriveled-up lobe?

Dr. Sweet: No; he saw a large round mass.

Dr. Burwell: It was within the right lung?

Dr. Sweet: Yes, in the region of the middle lobe. Unfortunately no biopsy specimen was taken.

I never entertained any thought of operating on the patient, but tried to establish a diagnosis. My conclusion was that he had a teratoma.

Dr. Burwell: No teeth could be seen in any of the x-ray films.

Dr. Sweet: No; however, I do not mean a dermoid cyst. A teratoma behaves differently from most of the dermoid cysts in the mediastinum that I have seen.

Dr. Castleman: I am sorry that Dr. Conger Williams is not here, but I shall read his note:

I am in favor of the diagnosis of pericardial effusion with tamponade to explain the findings of high venous pressure, paradoxical pulse and large cardiac shadow without evidence of valvular disease or anything to suggest diffuse myocardial involvement. Additional suggestive findings are left-border dullness 2cm. outside the apparent apex impulse and narrowing of the border of superior cardiac dullness on the left in the sitting position in comparison with the lying position. There is probably some displacement of the heart shadow to the left, but it does not account for the large cardiac shadow. The blood pressure of 108/78 is not especially impressive, but does not exclude the diagnosis. The fact that the heart sounds come through well does not rule out pericardial effusion. Also in favor of pericardial effusion, as against heart failure, is the fact that the patient can lie flat on his right side without dyspnea.

CLINICAL DIAGNOSIS

Teratoma of mediastinum, with extension to right bronchus and pericardium.

Pericardial effusion, with cardiac tamponade.

DR. BURWELL'S DIAGNOSIS

Malignant dermoid cyst of mediastinum, with extension to right bronchus and pericardium.

Pericardial effusion, with cardiac tamponade.
Pulmonary atelectasis and bronchiectasis.
Pleural effusion.

ANATOMICAL DIAGNOSIS

Carcinoma of the lung, with extension to pericardium, right auricle and pulmonary vein and partial obstruction to superior vena cava.

Pericarditis, acute and chronic, with hemorrhagic effusion.

Cardiac tamponade.

Pulmonary atelectasis, with cholesterosis, right middle lobe.

Hydrohemothorax, slight, right.

Pleuritis, chronic, fibrous, right.

PATHOLOGICAL DISCUSSION

Dr. Castleman: There was only about 100 c.c. of hemorrhagic fluid in the right pleural cavity, but most of the cavity was obliterated by dense fibrous adhesions. Most of the right lung was replaced by a grayish-white granular, soft tumor with many areas of necrosis, one of which formed a cavity measuring about 3 cm. in diameter in the lower lobe. The tumor involved the entire lower lobe and the lower four fifths of the upper lobe. The middle lobe was entirely collapsed and fibrotic and was mottled yellowish orange, owing to the large deposits of cholesterol. This so-called "cholesterosis" of the lung is not uncommon with long-standing bronchial obstruction. The middle and lower lobe bronchi were filled with tumor nodules. This tumor had extended medially to involve the right side of the pericardium, and the pericardial cavity contained a liter of bloody fluid. The visceral pericardium was covered with a shaggy brownish-red fibrinous exudate. The tumor apparently had extended through the wall of the parietal pericardium and had bled into the pericardial cavity. There was no actual tumor on the visceral layer, so that all this blood in the pericardial cavity was due to oozing from the tumor that had penetrated through the parietal layer. It had also penetrated through the right auricular wall into the auricle, obliterating a large part of its cavity, blocking the orifice of the superior vena cava, but without involving the endocardium. The tumor had also extended from the lung into the lower pulmonary vein for a distance of 4 cm. and had almost reached the left auricle. A photomicrograph taken through the right auricular wall shows tumor cells replacing the myocardial fibers. The tumor cells are epithelial in character. There is no stroma

between the cells, and without knowing anything about the story I am sure every pathologist would call this straight forward carcinoma of the lung. With the information that the tumor was of at least seven years' duration one might be justifiably skeptical of a diagnosis of carcinoma and might then bring up the diagnosis of endothelioma, possibly arising from the pleura.

Dr. Burwell: That would account for the extraordinary bleeding.

Dr. Castleman: Most of the tumors of the pleura diagnosed as endothelioma are carcinomas of the lung with extension to the pleura. In fact we rarely if ever make the diagnosis of endothelioma. The cases that have been reported as endothelioma usually have nodules all over the pleura and are associated with a hemorrhagic effusion. There were no nodules on the pleura in this case. Another theory of the origin of this tumor is that it arose from a bronchial adenoma. The right bronchi were filled with tumor, which may have been benign years ago and then became malignant, as a few of them do. We know that adenomas are prone to extend through the bronchial wall and form large extrabronchial tumors. Perhaps the tumor felt seven years ago may have been an adenoma. If that were true, it is strange that the patient had no hemoptysis.

Dr. Burwell: That is what troubles me.

Dr. Castleman: Nevertheless, I think we have to make a positive diagnosis at autopsy of carcinoma of the lung with extension into the pericardial cavity and into the heart. There was a metastasis to an intrapulmonary lymph node, close to the tumor, but no distant metastases.

Dr. J. H. Means: Would you grade it as a slowly growing malignant tumor because it has

been there for seven years? It must have been growing slowly.

Dr. Castleman: It was not rapidly growing, but certainly not slowly growing.

Dr. Burwell: Is that not an extraordinary duration?

Dr. Means: It does not seem possible that a carcinoma of the lung could have been present for seven years.

Dr. Castleman: I was also puzzled and showed these slides to two other pathologists, who agreed to the diagnosis of carcinoma.

Dr. Burwell: Suppose it had been an adenoma. Might it not have developed deep enough in the mucosa so that it went outward instead of inward?

Dr. Castleman: All the adenomas with extra-bronchial extension that we have seen also have a nodule of tumor protruding into the lumen, unless, of course, it had been removed bronchoscopically.

Dr. Burwell: It seems to me evident that whatever this was seven years ago, it was a carcinoma at autopsy. The problem that has to be settled is the presence of an obstructing lesion seven years previously that eventuated into a carcinoma of the lung.

Dr. Castleman: I believe that one can have a carcinoma of the lung of low-grade malignancy for seven years. A case that Dr. Allen discussed recently was a hepatoma of nine years' duration.* I think the whole idea of long-standing malignant tumors is something that we perhaps do not appreciate sufficiently.

Dr. Burwell: He had no hemoptysis.

Dr. Sweet: No; which suggests that the tumor did not arise in a large bronchus.

Dr. Burwell: That is one of the reasons why I thought of an extramural source.

Dr. Sweet: I was convinced all along, until I saw the autopsy, of mediastinal origin.

*Case records of the Massachusetts General Hospital (Case 29331). *New Eng. J. Med.* 229:342-345, 1943.

TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER, M.D.

The ODDEST TITLE of any book seen lately, medical or other wise, is by Dr. Reed Nesbit, noted urologist at the University of Michigan,—"Your Prostate Gland. Letters from a Surgeon to His Father" . . . In spite of the title it is a very fine book, one which you can well recommend to a patient confronted with a prostate lesion or a

need for prostatic surgery, and one which costs but two dollars. . . . The letters actually were written to the elder Nesbit, then collected and published—after he had had surgery.

Do you know the action of CITROVORUM FACTOR on aminopterin? Ten dollar medical words

but the meanings are interesting and could be important. . . . Aminopterin is one of the drugs which can inhibit the wild growth of blood cells (leukemia), but which may also destroy normal cells. . . . Citrovorum factor is a cousin of folic acid, discovered by Baumann and Sauberlich of the University of Wisconsin Ag. School, and named for a type of bacteria (*Leuconostoc citrovorum*) used in testing amino-acids. It may be obtained from liver extract. It is possible that folic acid must be converted to its cousin before animal cells can use it. The citrovorum factor contains a growth factor. . . . The answer to the first question is,—'The action of aminopterin is counteracted by the citrovorum factor'. It may be possible to give the new material to limit the effect of aminopterin in leukemia.

The COST OF HOSPITAL CONSTRUCTION is painful to consider, but a 500-bed clinical center at Bethesda, Maryland, hits an all-time high. Forty million dollars, or \$80,000 per bed! . . . Ten Thousand per bed was huge in 1950; \$20,000 per bed was high in 1948; but \$80,000 is high even for the gov'ment.

The Journal of Pediatrics contains the first large comparative series of antibiotics for PERTUSSIS. . . . Aureomycin, chloramphenicol, and terramycin are of equal value. They are not specific, but they reduce the duration of the whoop (or dangerous) stage by 60 per cent. Streptomycin was disappointing.

The Aero Medical Association has announced a 40-cent OXYGEN MASK for use in passenger traffic. It is made of white plastic and is disposable. . . . The proposed use is for rapid application in the rare cases when pressurization of the cabin is lost at high altitudes. Many of the patients would need help during the few minutes which would be required for the plane to lower to a safe level. . . . Strangely, the occurrence very seldom occurs, as was mentioned in an editorial on Air Travel in ARIZONA MEDICINE three years ago.

Preliminary reports on a therapy for MALE INFERTILITY comes from a good source—Dr. Carl G. Heller of the University of Oregon Medical School. He has been deep in this research field since before his internship in Wisconsin with Dr. Elmer Servinghaus. . . . He notes the need of therapy to improve fertility, since 2 of every ten young men have some deficiency in their sperm cells. . . . Sixty infertile men were treated for 6 weeks with 50 mg. of testosterone per day; 100 per cent favorable results followed. . . . A newer, quicker method has been found to be effective in 20 cases. The material is a pituitary gland hormone, called equine gonadotropin, and is obtained from the placenta of a horse. The restoration of sperm count seems to persist after treatment for as

long as 3 years. . . . Testosterone is applicable to more cases than the second method, which can be used only when the damage to sperm production is not too great.

THE AMERICAN DRUGGIST reports a poll of pharmacists on federal versus voluntary medical plans. Three fourths of those who replied favored the voluntary plan; only nine per cent favored the government-sponsored plan.

The use of high-energy, ELECTRONS to STERILIZE PACKAGED FOODS has had a great deal of publicity. The same method may be of value in medicine, since electron sterilization raises the temperature less than 5 degrees C . . . BLOOD, ANTIBIOTICS, ADRENAL CORTICOIDs, etc., are eligible for trial by the method. It has been used on surgical sutures (in ampoules) on a conveyor belt. . . . A cathode-ray sterilizer is used. Various types of bacteria have been exposed to varying doses, and the effective exposures are becoming known. . . . The composition of the substances is not changed when the exposure is specifically arranged. . . . It also seems possible that tissue transplants can be sterilized before use—an exciting potential of the method. . . . Machlett Laboratories has worked on the project with Dr. John Trump of M.I.T.

Sic Transit Gloria—The names of physicians who are gone are too soon forgot. The ancient ones can be recalled by very few, and the recent ones are fading fast. . . . What is needed is A MEMORIAL which will meet the eye, year after year. . . . There are at least two approaches,—the hospitals might arrange for it, or the county medical societies could do it. Plaques would be the easiest, but the most ignored and silent method. . . . We favor having each county medical society choose a list of 6 to 12 names; then label a lecture each month, or every other month, with the name of a physician. Money must be spent anyway to pay expenses, and it would be a kind and thoughtful act to keep a memory fresh. . . . Tucson, e.g., could have a Victor Gore Lecture, a Samuel Watson Lecture, and events named for the late Drs. Patterson, Charles Wilson Mills, Davis, Kibler, and a half dozen others to be chosen by a committee of elder senators—while there is someone who remembers.

The fabulous record of Dr. Mathra Das, one of India's leading eye surgeons, is published by the Medical Society of New Jersey. Up to the first of January, 1946, Dr. Das had done 188,663 CATARACT OPERATIONS. His record for a single day was 707 extractions. . . . It would fatigue most people to shake hands with that number. . . . No data were given on the incidence of infection or on the end results.

The following note may be 'significant',—The

National Association of COLORED GRADUATE NURSES has disbanded. Founded in 1908, the Association believes that its promotional function is no longer necessary. . . . Negroes are integrated into the nursing profession in many hospitals, public health agencies, and the armed services. The tendency is increasing.

New estimates of the values of 'ANTABUSE' are gradually appearing. . . . Early reports were encouraging; succeeding reports showed its toxicity and limitations; and a new paper by Wexberg and colleagues in the Medical Annals of the District of Columbia show its adjunct value. . . . They deny that it produces a conditioned reflex. The illness caused by an Antabuse-Alcohol combination is regular and biochemical. . . . They use it as an adjunct to psychotherapy; in 20 patients the effect was good and there were no untoward results. They also quote another careful series from New York of 150 cases in which there were no ill effects.

The March 'Hospital Topics and Buyers' Guide' quotes Dr. R. G. Kesel on DENTAL CRIES CONTROL PROGRAMS. He ought to know, since he is the University of Illinois professor who helped invent ammoniated tooth-paste. . . . Dr. Kesel says that there never will be an effective program until something can be introduced into routine living which will not require thought, action, or denial. . . . He favors fluoridation as a practical method. In addition, sugar consumption should be moderated, tooth-brushing after meals should be diligent, sodium fluoride may be applied to the teeth, and perhaps ammoniated dentifrices may be helpful. (He suggests that the last-named is not yet well enough tested).

DRUG ALLERGY may show itself by spikes of fever, abdominal pain, and a dermatitis. . . . The symptoms of fever (malaise, fast pulse, anorexia, sweating, etc.) may add to a diagnostic confusion.

The huge chore which is involved in opening A NEW MEDICAL SCHOOL is nearly complete in Los Angeles. THE UCLA MEDICAL SCHOOL will open for the first class September 19, 1951. . . . Dean Stafford L. Warren has assembled a faculty, obtained space, and arranged the curriculum. The housing will be in temporary structures. The hospital facilities include the Harbor General (750 beds), the Sawtelle V.A. Facility (1,500 beds), and the Long Beach V.A. Facility (1,500 beds). . . . Dr. Warren has drawn heavily on

the University of Rochester, where he was once professor of radiology. He has 22 fulltime faculty members, 98 clinical appointees. . . . Dr. W. P. Longmire Jr. of Johns Hopkins is Surgical Chief, and Dr. John S. Lawrence of Rochester is Chief for Medicine. . . . A UCLA Medical Center is being built by 1953 at a cost of \$15,500,000.

The mechanism of action of ACTH and Cortisone on most of the SKIN DISORDERS which respond is still uncertain. According to present concepts there is no evidence of hormone deficiency. The theory has to be constructed so that an excess of hormone is required to produce favorable results. . . . It will be interesting to see how it turns out.

The displacement of DR. MAGNUSON from the V.A. chief medical directorship could open the service to the same flaws which are said to be present in English practice and hospitalization. . . . Dr. Magnuson says that he was fired. He says that it is part of someone's plan to run the V.A. by beaureaucracy. . . . Dr. Paul Hawley ways that the department has lost its prop and "will fall into the gutter". . . . It is hoped that the Humphrey Committee will spell out the chief's duties so that the 'old' V.A. cannot return.

The syndrome of HYPERVENTILATION should be remembered, since the cause is not an obvious one and the symptoms do not point to overbreathing. . . . It includes headache, light-headedness, dizziness, constriction around the chest, dyspnea, palpitation, and numbness and tingling of the extremities. . . . Nervousness, tension, and anxiety are predisposing states.

Dr. Clarence Mills of Cincinnati, famed expert on climatology, tropical diseases, clean air, etc., has gone beyond the cigarette advertisements to clarify THE BIOLOGIC HAZARDS OF SMOKING. His article in The Ohio State Medical Journal turns on the red stop-light. . . . Acute and chronic nicotine poisoning are serious effects. They result from ganglionic cell poisoning, with a stimulative-irritative-paralytic effect. . . . The diseases in which tobacco smoking may be a factor include thrombo-angeitis obliterans, peptic ulcer, respiratory tract cancers, reproduction and lactation in women, and other respiratory diseases. The information probably won't change the public's habits, but it could help the physicians' attitude.



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Reprinted from J.A.M.A., May 12, 1951.

Left to Right: Dr. Russel V. Lee, Palo Alto, Calif.; Dr. John M. Murray, Boston; Dr. Cortez F. Enloe, Manhasset, Long Island; General Armstrong; Dr. Herbert B. Wright, Cleveland; Dr. William P. Holbrook, Tucson, Ariz., and Dr. Elmer L. Henderson, Louisville.

AIR FORCE

Inspection Tour in Korea.—Maj. Gen. Harry G. Armstrong, Air Force surgeon general and Brig. Gen. Albert H. Schwichtenberg, chief, Civil and Military Inter-Relation Division, Office of the Secretary of Defense, have returned from an inspection of the Air Force medical facilities in the Far East. Other military personnel in the tour included directors and top level chiefs of the Surgeon General and representatives of the School of Aviation Medicine.

Civilian consultants making the trip were Dr. Cortez F. Enloe, Manhasset, L. I., N. Y., internal medicine; Dr. Elmer L. Henderson, Louisville, surgeon and President, American Medical Association; Dr. William P. Holbrook, Tucson, Ariz., internist and president, American Rheumatism Association; Dr. Russel V. Lee, Palo Alto, Calif., internal medicine; Dr. John M. Murray, Boston, psychiatrist, and Dr. Herbert B. Wright, Cleveland, urologist.

A headquarters press conference was called April 5 by General Armstrong. Dr. Holbrook said, "We visited dispensaries, hospitals, airstrips, talked to pilots of fighters and bombers; followed the medical chain of evacuation from the front on back through the chain, and talked to hundreds among the group who were then well and doing the fighting. At present the three services—Army, Navy, Air Force—are giving the best care that has ever been given to the troops, with less than half the doctors per thousand troop population used during the last war."

Dr. Henderson flew 80 miles over the enemy

lines in Korea and rode an air evacuation plane carrying patients from Korea back to Japan. "Their morale," he said "was very high." A lieutenant remarked, "Five minutes after I was wounded I was back in the first-aid station where I was taken care of. My wounds were dressed, and within 50 minutes I was on a plane being evacuated by air to a hospital in Korea." Air evacuation is the greatest thing that has come out of this Korean incident as concerns saving lives of soldiers."

Dr. Enloe said, "I ran into five soldier-patients at Travis Air Force Hospital in California on March 17. On March 7 they had been wounded prisoners of the Chinese. They were released by our advance on the seventh and within 10 days were in California."

Dr. Lee checked particularly on young military doctors "I think I found only one out of something over a hundred physicians who was dissatisfied with his particular assignment," he reported. "I thought we would get a lot of complaints from these young doctors, but the contrary was true. They were all happy and glad to be doing their job. In other words, the medical morale was extraordinarily high."

According to the physicians who made the tour, as of March 31 a total of 112,000 United Nations personnel have been airlifted in the Korean action with not one injury or death occurring due to air evacuation. This figure included all UN casualties, also persons lifted several times, as well as persons hurt from causes other than battle injuries. Twenty-two thousand American casualties have been airlifted from the Pacific back to the United States.

DR. NELSON D. BRAYTON

Miami, Arizona

(Response to the Address of Welcome at the 60th Meeting of the Association at Tucson, Arizona. Member of the 50 Year Club of the Arizona Medical Association.)

Mr. President, Members of the Medical Association, Members of the Pima County Medical Society, Friends:

There is an old saying that Truth in Medicine is like the Venus de Milo of the Louvre in Paris — She wears no clothes.

So, in this great, though still young city; yet by nomenclature called the OLD PUEBLO, we again accept your welcome, and the always pleasant invitation for our scientific, cultural, educational, and social meeting—this one the 60th in the annals of our association.

A moment ago I said that Truth wears no garments; she needs no dressing up. Like Science, she recognizes no boundries, she knows no Frontiers. In education the sky is her limit. And of Old Tucson we know that we can say hospitality is just as uncovered; just as limitless; just as boundless. Especially do we appreciate the hospitalities already shown and being shown

by your gracious ladies to our own ladies. In the same way we appreciate, and we accept, of the advances—your local advances—in engineering, in the arts, in education, and especially in the architecture of the human soul which is the ever expressive and constant natural growth of Tucson's own fine citizenship.

And in return for this fine compliment of your fine hospitality and to this welcome from your heart, the Arizona Medical Association pledges itself to the further solutions of the problems of Public Health and your Health; to the problems of personal illness, injury and disease; to the problems of Scientific, Therapeutic, and Pharmacologic advances of the future; to those great problems in the study of Human Relations and the Personal Dignity of Man; and to the Recognition, without appreciation of the PRESS in presenting, in its fairminded way, our problems to the Public.

Especially in this meeting do we again dedicate ourselves to the sanctities of the problems of the POOR. In our endeavors to worthily compliment your hospitalities and your Welcome, I SAY TO YOU "THE ARIZONA MEDICAL ASSOCIATION WILL NOT FAIL."

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BASAL METABOLISM

R. Lee Foster, M.D., Director

John W. Kennedy, M.D., Radiologist

W. W. Watkins, M.D., Consultant Radiologist

Diplomates of American Board of Radiology

SCHERING AWARD WINNERS ANNOUNCED

Dr. S. I. Griboff, senior medical student at Syracuse University College of Medicine when he enrolled in the competition, has been announced as the winner of the "Schering Award for 1950." Dr. Griboff is now serving his internship at Mt. Sinai Hospital, New York City. Mr. Francis C. Brown, president of Schering Corporation, presented the first prize of \$1000 to Dr. Griboff for his paper on "The Clinical Use of Steroid Hormones in Cancer."

Co-authors Robert W. Winters and Henry M. Williams, both third year students at Yale University School of Medicine, were tied with Kenneth J. Ryan, third year student at the Harvard Medical School, for second prize and were awarded duplicate prizes of \$500. Monte J. Meldman, third year student at Marquette University School of Medicine, was awarded the third prize of \$300. Twenty-five contestants received honorable mention, and each received special awards in acknowledgment of their contributions.

The Schering Award is given annually for the best manuscripts prepared on designated phases of endocrinology. Medical students of the United States and Canada are eligible for the contest. The majority of medical schools are represented by applicants.

Each year three physicians prominent in the clinical field covered by the subject act as judges for the Schering Award Competition. The judges for the 1950 Award were Dr. Ira T. Nathanson, Assistant Professor of Surgery, Harvard Medical School; Dr. Cornelius P. Rhoads, Director of the Memorial Center for Cancer and Allied Diseases, New York City; and Dr. Walton W. Van Winkle, former Secretary of the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association.

THE ARIZONA MEDICAL ASSOCIATION, INC. ARMED FORCES SERVICE ROLL

The following members of this Association have entered Military Service to July 1, 1951:

KINGMAN

BARNES, Broda O., M.D.

MESA

KRIPKE, Morton J., M.D.

MORENCI

SABA, Phillip Z., M.D.

PHOENIX

BAILEY, PERRY W., M.D.

CLAYPOOL, Lewis B., M.D.

FURTH, William G., M.D.

LONG, David R., M.D.

O'CONNER, Jeffrey A., M.D.

STEFFANS, Henry J. J., Jr., M.D.

SAFFORD

KELLER, Robert S., M.D.

TEMPE

GUTEKUNST, R. A., M.D.

TUCSON

DAVIS, James W., M.D.

HELDOBLER, Alfred O., M.D.

OVERMAN, William E., M.D.

RIGGALL, Jack L., M.D.

WICKENBURG

SHANNON, Frederick A., M.D.

WILLIAMS

LAWSHE, Roger D., M.D.

YUMA

LAYLAND, Calvin H., M.D.

STRATTON, Robert A., M.D.

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BLUE SHIELD

Dr. Carlos C. Craig, Phoenix, was re-elected president of Arizona Blue Shield Medical Plan for a second term at the annual Board of Directors meeting held April 29, at the Pioneer Hotel, Tucson.

Other officers re-elected at the Board meeting were: Dr. E. A. Born, Prescott, Vice-President and Mr. Earl Barrows, Phoenix, Treasurer. Dr. David C. James, Phoenix, was elected Secretary.

Newly elected to the Board of Directors at the same meeting were: Dr. James and Dr. Zeph Campbell of Phoenix, and Dr. Robert Hastings, Tucson. Re-elected were Barrows and John Durkin of Tucson. Continuing on the Board are: Reverend George Ferguson, Tucson; Dr. Walter Brazie, Kingman; Dr. Royal Rudolph, Tucson; Dr. Craig; A. W. Liddell, Bisbee; Dr. Robert Cummings, Phoenix; Dr. O. E. Utzinger, Ray; John Babbitt, Flagstaff; and Dr. A. I. Pololsky, Yuma. Dr. Campbell was elected to serve on the Executive Committee along with the four officers for the coming year.

Dr. Kenneth B. Brillhart, Cottonwood, and Dr. L. Clark McVay, Phoenix, were elected to the Professional Committee. Others serving on the Committee are Dr. H. D. Ketcherside and

Dr. J. M. Greer, Phoenix, and Dr. Edward Hayden, Tucson.

As a means of informing the public in general and Blue Shield subscribers in particular of the financial stability, the soundness of investment and the amount of services rendered Arizona Blue Shield members by Participating Physicians during the past year, the illustrated message on the foregoing page was published in various newspapers throughout the state.

BOOK REVIEWS

Handbook of Pediatric Medical Emergencies. By Adolph G. DeSanctis, M.D., Professor of Pediatrics and Chairman of the Department of Pediatrics, Post-Graduate Medical School, New York University—Bellevue Medical Center; Director of Pediatrics, University Hospital, New York University—Bellevue Medical Center; Director of Pediatrics, Gouverneur Hospital, New York City, and Charles Varga, M.D., Instructor in Pediatrics, Post-Graduate Medical School, New York University—Bellevue Medical Center; Assistant Attending Pediatrician, University Hospital, New York University—Bellevue Medical Center; Assistant Visiting Pediatrician, Gouverneur Hospital, New York City. Price \$5.00. Pp. 284, with 51 illustrations. C. V. Mosby Company, 3207 Washington Boulevard, St. Louis 3, Missouri, 1951.

It is quite obvious when looking through this book that it is designed for the medical student, the interne and the resident in pediatrics. Any medical student or interne particularly during his pediatric service, would be very happy, I think, to have such a volume as this. It is small in size making it easy to carry and covers the subject for which it was intended rather completely. The various medical emergencies encountered in pediatric practice are arranged for easy reference and the information is given in abbreviated and tabular form in most cases. The typographical arrangement is excellent for this type of reference, the various emergencies being titled in large, bold, capital type with the pertinent information arranged in outline form below it. This makes it very easy to find any particular subject quickly which is important in the practical use of this type book.

The various pediatric diagnostic and therapeutic procedures are excellently illustrated and should be very valuable to the physician who wishes to refresh his memory or some infre-

quently used procedure as well as for the teaching of new procedures to the interne and resident.

One useful feature is the large list of ordinary household cleaners, insect killers and other household chemicals with information as to the poisons which they contain and a rather complete outline of treatments for these various poisons.

Since any physician, whether he does pediatrics or not has a fairly good chance of being called at some time to act in a pediatric emergency, it would seem that this book would be a practical addition to the physician's library.

The Science of Health, second edition, by Florence L. Meredith, B.Sc., M.D., Fellow of the American Medical, American Public Health and American Psychiatric Associations. \$3.75; 48 Tables and Charts; 134 illustrations; 452 pages, January 3, 1951. The Blakiston Company, 1012 Walnut Street, Philadelphia 5, Pennsylvania.

This book according to the preface by the author is intended for use as a textbook in hygiene courses and would seem to fulfill that function quite well. It presents a good over-all view of the health situation as it applies to the nation and to the individual without entering into tedious detail on any particular item. The book is divided into five main parts, the first being the Introduction and dealing with the national health situation and a general view of the structure of the body. Part two is entitled Daily Maintenance of Health and has to do chiefly with personal hygiene. Part three is entitled Major Health Problems in the United States and deals with the public health situation. Part four is entitled Mental Health and deals not only with the physical care of the nervous system but also with the mental and personality portion of health. There is a chapter entitled the sex impulse. Part five is entitled The Next Generation and has to do with reproduction and with heredity and parental care. A good bibliography is included which should be an excellent guide for further and more detailed study and the index is quite satisfactory.



PERSONAL NOTES

The following Phoenix doctors attended the American Medical Association Annual Convention in Atlantic City, New Jersey, June 1951: *Dr's. Joseph Bank, DeWitt W. Englund, George S. Enfield, Robert S. Flinn, Jesse D. Hamer, Wallace Meyer, and M. James Whitelaw.*

At the May 28th meeting of the hospital Staff at Good Samaritan Hospital, a program was presented by the hospital house staff. *Dr. James Shoun* spoke on "Diagnostic Pitfalls in Lupus Erythematosus." *Dr. Lloyd A. Owens* reported "Two Cases of Untoward Reactions Following use of Intravenous "B" Complex," and *Dr. C. Thomas Disney* presented "An Evaluation of Internship at Good Samaritan Hospital."

At the June Maricopa County Medical Society Meeting held June 4, 1951, at the Good Samaritan, a new constitution and by-laws of the Society was adopted, and a loan plan for doctors with hardship going into military service from the County Society. *Dr's. Oscar W. Thoeny and Archie Cruthirds*, Phoenix, gave reports of the County and State Hearing Conservation Committee.

Mr. Frederick G. Mitten, formerly of New York City has been chosen executive-secretary of the Maricopa County Medical Society, and was introduced formally to the membership at the June meeting. He has visited the Santa Clara and Alameda medical societies to survey their programs in behalf of improving medical public services.

Dr. David James, Phoenix, gave a Review of Gall Bladder Surgery for 1950 at the June 11th St. Joseph Hospital Staff meeting. This excellent review was discussed by *Drs. Karl Harris and J. H. Patterson*, Phoenix.

The Memorial Hospital, Phoenix, Arizona June staff meeting was held June 18, 1951. Following "Review of Autopsies" by *Dr. Maurice Rosenthal*, Phoenix, "An Unusual Kidney Stone Case" was presented by *Dr. Paul L. Singer*, Phoenix. *Dr. Otto Bendheim*, Phoenix then reported "Some Clinical Experiences with "Anti-Abuse."

Dr. John R. Green, presented "The Surgical

Therapy of Focal Epilepsy" with a film at the June 25th Good Samaritan Staff meeting.

Dr. Edith Lord, Phoenix, Director of the Mental Health Division State Department of Health, attended the Western Psychological Association meeting at San Jose, California, where she presented "Personality Changes with Han-son's (leprosy) as Measured by the Ronschaeh Ink Blot Test."

The following doctors attended the April meeting of the American College of Physicians in St. Louis April 1951: *Dr's. Joseph C. Ehrlich, Leslie R. Kober, Kent H. Thayer, and O. O. Williams*, Phoenix. *Dr. Lipschultz* of the Phoenix Veterans Administration attended this meeting, as did *Dr. Walser* of Whipple, Arizona. Some Tucson physicians attended this meeting, but the editor does not know of their identity.

Dr. R. Lee Foster, Phoenix, has taken over direction of what was formerly the Pathological Laboratory in the Professional Bldg., Phoenix, and is operating it as "Professional X-ray and Clinical Laboratory" with *Drs. J. W. Kennedy, and W. W. Watkins*, Phoenix, as associates and consultants.

An Arizona Chapter of the Fellows of the American College of Surgeons, has been organized. Officers were elected as follows: *Dr. Meade Clyne*, Tucson, President; *Dr. Norman Ross*, Phoenix, Vice-President; *Dr. Clyde E. Flood*, Tucson, Secretary-Treasurer. Councilors are: *Dr. Joseph M. Greer*, Phoenix, *Dr. Clarence H. Tucson.*

Kuhlman, Tucson, and *Dr. Royal W. Rudolph*,

Dr. George S. Enfield, Phoenix, has been elected a Fellow of the American College of Anesthesiologists."

Dr. Marcy L. Sussman, Phoenix, has been elected to membership in the New York Academy of Sciences.

Dr. William Snyder, Phoenix, has been appointed by *Dr. Donald Pillsbury* to the University of Pennsylvania Service at the Skin and Cancer Hospital of Philadelphia. He begins this residency July 1, 1951 upon completing his second year as resident in Dermatology at the Cincinnati General Hospital.

SECRETARY LULL'S LETTER

May 14, 1951

That medical science has no boundaries certainly is exemplified in the recent travels of our President, Dr. Elmer L. Henderson. In serving the Association, during the past year Dr. Henderson has traveled approximately 100,000 miles.

A few weeks ago he was flying over enemy lines in Korea. Last week found him in Geneva, Switzerland, at the council meeting of the World Medical Association, of which he is president. He was accompanied on this last assignment by Dr. Louis H. Bauer of Hempstead, N. Y., Secretary General of the W.M.A. and Chairman of the A.M.A. Board of Trustees, and Dr. R. L. Sensenich of South Bend, Ind., a member of the council and Past President of the A.M.A. Following the council meeting, Drs. Henderson and Sensenich accompanied an Air Force mission to Germany and France.

The best way I know of reporting to you on what transpired is to let you read part of a letter just received from Dr. Henderson:

"Our trip by air was uneventful except for an unexpected stop at Goose Bay, Labrador, a military installation of the Royal Canadian Air Force. While awaiting the refueling of the plane we chatted with Dr. Joseph Carroll, flight lieutenant for the Canadian Air Force. He said the biggest health problem in that remote spot, where the temperature drops to 33 below in winter and climbs to 100 in summer, is tuberculosis in Eskimos. Every day, they come trekking into his small post hospital. Most of the cases are in advanced stages.

A polio outbreak a year ago brought more than 30 natives to the hospital in less than two weeks. The cases were transferred to Halifax for treatment.

"We arrived in Geneva via Paris and found the meeting of the Council of the World Medical Association stimulating and worth-while. By authority of the General Assembly, granted at the New York meeting last October, the council elected the Japan Medical Association and the Western German Medical Association to membership in the W.M.A. Japan has 55,000 doctor members and Western Germany has 60,000.

"It was made clear that both of these organizations had denounced war crimes and would abide by principles contained in the Declaration of Geneva.

"With Japan and Western Germany, the World Medical Association now comprises 42 national medical associations with a combined membership of well over 500,000 physicians. New membership applications have been received from several other countries, including Latin American and Asian.

"One day of the council meeting was devoted entirely to a discussion of finances. Several council members, including President-Elect Dag Knutson of Sweden and Dr. Otto Rasmussen of Denmark, expressed appreciation for the financial help extended by the American Medical Association to the World Medical Association.

"We owe the doctors of America a great debt of gratitude for the help they have extended since the association's founding in 1947," Dr. Knutson said.

"After the council adopted a resolution expressing its appreciation of the financial help extended by the United States Committee and the A.M.A., a committee was appointed to study and make recommendations as to the financial affairs of the organization. The four committee members are: Treasurer Otto Leuch, Switzerland; Dr. Rasmussen of Denmark; Dr. J. A. Pridham of England and Dr. L. Garcia Tornel of Spain.

"Dr. Bauer and I were pleased that the European countries are particularly anxious to assume a greater proportion of the financial burden. One of the biggest drawbacks, however, is that under present financial restrictions it is impossible to get money out of some of the countries. The newly-appointed committee will work on this phase of the problem, with the hope of finding a solution.

"The council members were guests at a reception tendered by the International Committee of the Red Cross, whose headquarters are in Geneva. Located in a neutral country, the International Red Cross is particularly qualified to act on humanitarian matters during wars. In World War II it opened a central prisoners of war agency in Geneva and by the end of 1946 its card index for prisoners of war and civilian internees contained some 39,000,000 names. The staff comprises about 4,000 persons, including 1,000 volunteer workers.

"On another evening, we were dinner guests of the Geneva Medical Association at an age-old inn nestled in a forest near the snow-capped Alps. There were many speeches, excellent

food and sincere exchanges of friendship. I stressed the importance of these World Medical Association meetings in furthering the cause of medicine throughout the various countries.

"The trip has been most enjoyable, although a bit tiring at times. We have been tendered gracious hospitality."

"*Today's Health*" voted public interest award. Dr. W. W. Bauer, editor of *Today's Health*, was informed by the National Safety Council recently that the A.M.A. publication was one of six magazines in the general publications field to receive the council's Public Interest Award for 1950.

Mr. Ned H. Dearborn, president of the National Safety Council, in his letter to Dr. Bauer, said in part: "We are proud to confer this public recognition for exceptional service to safety, and are extremely grateful to you. There is no doubt your efforts have helped to prevent many accidents and saved lives."

I've just completed reading an article by Paul de Kruif in the June issue of *Reader's Digest*. It knocks into the proverbial "cocked hat" the piece entitled "Our Alarming Doctor Shortage," which recently appeared in another national magazine.

In fact, the de Kruif article is so good—and it should carry a great deal of weight because of the international reputation of the author—that the American Medical Association has taken steps to see that it gets into the hands of every doctor in the United States.

And, with the help of the medical profession, the article can come to the attention of millions of people aside from the 6,000,000 who are subscribers to the *Reader's Digest*.

Consequently, the A.M.A. has obtained reprints of the article. A copy will be sent to every doctor, advising him that additional reprints for his waiting room may be obtained through the state medical society. County society secretaries will be able to obtain their supplies through the same sources. We should make every effort to place a copy of this article in the hands of every molder of public opinion.

DeVoto Article Also Receives An Answer. *Harper's* magazine recently carried an open letter by Bernard DeVoto to his doctor. DeVoto

said he was deducting 25 cents from his check in payment of his doctor's bill because he did not believe in contributing indirectly toward the \$25 which the doctor had sent to the A.M.A. The letter was hailed by socialized medicine proponents as presenting an excellent idea.

The Freeman, in its April 23 issue, likewise thought the plan was a good one and should be applied to other bills. For instance, the magazine suggested, it could be applied to our income tax bill. If we don't believe the R.F.C. should lend its money for certain purposes, or that government funds should be used to raise our food costs or to pay some bureaucrats salaries, well, just make deductions from our tax payments. The only drawback, as the *Freeman* pointed out, is that the government could put us in jail.

Nevertheless, the article serves to show just how ridiculous some proponents of socialized medicine can get.

This Year's Clinical Session Moved to Los Angeles. Due to conflicting meetings, the unavailability of the Coliseum and other considerations, the 1951 Clinical Session will be held in Los Angeles instead of in Houston, as planned originally. The action was taken upon the recommendation of the Local Medical Committee on Arrangements and the Texas State Medical Association. Los Angeles was selected by unanimous vote of the Board of Trustees. The dates will remain unchanged—December 4 to 7, inclusive. The scientific exhibits will be in the Shrine Convention Hall.

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X-ray machine used less than 6 months, Westinghouse 100kc.—100 M.A., Bucky, Vertical and horizontal fleuroscopy. All accessories included such as large developing tank, 3 cassettes, lead apron and gloves, viewing box etc., all new. Purchase price \$3,500. Ask \$1,995 F.O.B. Northern Texas. Reason for selling, ill health. Address in care of

ARIZONA MEDICINE JOURNAL
426 Heard Building
Phoenix, Arizona

WOMAN'S AUXILIARY



MRS. ROYAL W. RUDOLPH

INAUGURAL ADDRESS

During the past year, each day has brought to me, as your president-elect, a stronger realization of the tremendous responsibility ahead. I could not help feeling inadequate for the honored position which you, today, have bestowed upon me. But knowing the confidence which has been shown in electing me, I have tried very hard to equip myself and now pledge that I will carry on as president of the Woman's Auxiliary to the Arizona Medical Association to the best of my ability. I wish to pay tribute to Mrs. Herzberg for her splendid leadership this past year and sincerely thank her for the time and energy she has spent to give me a better understanding of auxiliary work. I am grateful to the new officers and committee chairmen who have accepted their posts and pledged their support for the coming year. We are privileged to have with us today our National President, Mrs. Herold, whose message, as always, will be a great inspiration to us all.

America is the country it is today because there has been freedom of opportunity. People wanted freedom; they worked, sacrificed and fought for it. Then came the tendency to take

the American Way of Life for granted. Rather than lose it by carelessness and indifference, we have been awakening to the fact that our freedom is endangered. We must work harder and sacrifice more to keep this heritage. The responsibility is not for a few; every American woman can do her part through some chosen channel. We as doctors' wives are privileged to extend the aims of the medical profession to all organizations which look to the advancement of health and health education.

What can we do as individuals? Our first step is self-education. Reading *Medical Journals*, our *Bulletin*, *Arizona Medicine* and *Today's Health* will familiarize us with the background and current happenings in medicine. County programs aim to give members a better understanding of all local problems, and to include a briefing of both state legislation and national legislation incorporated in the Capitol Hill reports from Washington. It is hoped that from time to time we may pass on to our membership a summary of information received from the National Educational Campaign in order that our members can keep abreast with the progress being made by the A.M.A. in its fight against socialized medicine. Members-at-large and members of component auxiliaries can keep well informed through their own organization by reading and by attending meetings.

By accomplishing this first step of self-education, we are preparing for the second because infiltration of informed people is the key to successful public relations. The county reports read this morning show that Arizona's Medical Auxiliary has had an active public relations program, much of which will be continued next year. One of the most important parts of this has been the Student Nurses' Loan Fund. If the war continues, the shortage of nurses may become acute and our program stepped up. The field of Civil Defense confronts us especially as doctors' wives. Throughout the country many of our members who are nurses are offering their services as teachers; all members are urged to join classes so should an emergency arise, we shall be prepared to aid our husbands in their community responsibilities.

With the approval of the Doctors' Advisory Council, the Public Relations and Health Committees hope to combine efforts in sponsoring a Health Education Program in Arizona through the media of radio and film. Each component

auxiliary will vary the program according to its special community needs. I am sure that members-at-large also will see ways in which their communities can benefit from this project and I hope they will not hesitate to approach the state chairmen for helpful information. Though this Health Education Program may have to start on a modest scale the first year, it holds tremendous possibilities for the future.

In conclusion, may I ask if you, this day, will pledge yourself to do the following things this coming year?

1. Become a member of the auxiliary by paying your dues.
2. Subscribe to and read the *Bulletin* and *Today's Health*.
3. Read *Arizona Medicine* when it comes to you each month.
4. Attend your county and state meetings. Will you evaluate the work that can be accomplished with collective effort by the Medical Auxiliary in the rural areas, in the communities and in the state? If you believe in its value, will you set aside part of your time to aid our auxiliary in its effort to be of service? No country can be stronger than its states. No state can be stronger than its communities. No community can be stronger than its members. And, likewise, this is true in our organization; our auxiliary will be as strong as you and I make it. True, it takes reliance, resourcefulness, initiative and courage but with it all, will come the joy and inner satisfaction of worthwhile accomplishment.

Mrs. Royal W. Rudolph
State President

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**SUMMARY OF BILLS BEFORE
CONGRESS ON FEDERAL AID TO
MEDICAL EDUCATION**

There are seven bills in Congress which would provide federal subsidies for medical schools. One is in the Senate (S.337) and the others are in the House of Representatives. The common denominator, or theme, in all is a presumption that there is a shortage of physicians which can only be overcome by subsidizing medical schools with federal funds. To accomplish the objective, several approaches are outlined in these bills.

S-337 goes beyond the common theme by stressing the defense needs of the nation. Its method

of approach is through aid to medical, dental, nursing, public health, osteopathy, and allied technical schools. This bill had bipartisan support in the Senate Committee on Labor and Public Welfare and was reported out by unanimous consent of its members. Objection has been raised repeatedly when it has been called up on the Unanimous Consent Calendar. Technically it may be considered at any time. Two of the House bills, H.R. 1781 and H.R. 2707, are identical with S. 337.

Another approach—through grants for construction only—is contained in H.R. 2152 which also adds to the common theme by stressing national defense and security.

A quite different approach to the common objective is contained in H.R. 3371, which would in effect turn the whole program over to the National Science Foundation. The Foundation would be authorized to work up a 5-year program for federal aid to medical schools, to students, and to faculties. The program and administration would be left entirely to the Foundation after approval by Congress.

A variation on the theme is the proposal of H.R. 3511, which would create a corporation within the Federal Security Agency called the "Medical College of the United States". Graduates would be compelled to serve in either the military or some federal service for a stated period—failing to do so they would be obligated to reimburse the government a part of the cost of their education.

Another bill creating a new medical school for producing physicians for governmental service is H.R. 3931. This school would be called the "United States Medical Academy". On completion of training, each student would be commissioned and required to serve five years in the military or some other federal service.

The American Medical Association opposes the passage of all these bills. Any program of grants in aid to medical education has far reaching implications with respect to the freedom of the medical schools. Financing of medical schools when not undertaken by private organizations should be a responsibility of the state. The establishment of a Medical Academy or Medical College of the United States, would not overcome the shortage of physicians, presuming there is such a shortage.

It is quite apparent that the features of these bills will be extensively discussed, especially

S. 337, and you can be of material help to your legislators by sending him the following:

1. Your reasons for opposing the bill.
2. Such documents as you may have in support of the position you have taken.
3. Your knowledge as to whether there is, or has been, a shortage of physicians in your area.
4. In your opinion, if the medical school in your state (if we had one) were in need of financial assistance, should the aid be given through federal subsidies or increased state appropriations.

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PROPOSED PUBLIC RELATIONS AND HEALTH PROGRAM FOR 1951-1952

It is our great hope to inaugurate, in Arizona, a program of Health Education patterned from the "Healthy Living in our County" project developed by the State University of Texas, with the cooperation of 23 organizations and agencies interested in the promotion of a constructive health education program, based on radio broadcasts, but using movies and posters as well.

After two years of successful experience, they now have complete material for the organization and execution of this program, available to any state interested in adapting this project to its own use. The major expense in promoting this plan would be the printing and distribution of the materials.

Briefly, the plan is as follows: All programs revolve around a quiz session in which teams of fourth, fifth, and sixth grade children from two schools compete in an attempt to answer the most questions asked by a master of ceremonies about a given health subject. A visiting expert in the health field under discussion acts as judge in case of dispute. Classes in the competing schools, those in other participating schools, and many parents listen regularly to the broadcasts, and preparatory and follow-up sessions under the supervision of teachers adapt each health subject to the local situation.

Acceptance of the "Healthy Living" program has been universal. School children have fun taking part in and listening to the shows. Teachers find health an easier subject to get across to their charges. Parents appreciate the better health habits of their sons and daughters and privately are proud of their own increased knowledge. School, home and community facilities reflect wiser health attitudes. It is im-

possible here to go into detail about the scripts for "Healthy Living in Our County", the procedures to be followed, (in arranging with schools and radio stations for its production), and the specific results which accrue from the program.

"Healthy Living in Our County" is a positive approach to health education, providing factual information for youngsters in a form pleasing to them and creating a community interest in health which consistently results in better habits and better facilities. Arizona State Medical Auxiliary would search a long time for a better project to support, for in encouraging this program, physicians' wives (and physicians, too) can demonstrate their desire to enhance health standards and performance within their communities.

Necessary Steps to be Followed in Order to Inaugurate "Healthy Living In Our County" Program

1. Someone (preferably a doctor) to present program to University of Arizona to enlist its sponsorship.
2. Approval of School Superintendents, and their cooperation in placing "Health Education" in their program.
3. Cooperation of Radio Stations.
4. Cooperation of other health, welfare, and civic agencies.
5. A financial plan for necessary expense of printing and distribution of materials.

Mrs. Joseph M. Kinkade
Mrs. Kenneth C. Baker
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1. Jeans, P. C.: Feeding of Healthy Infants and Children, J.A.M.A. 142:806 (Mar. 18) 1950.

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AUGUST, 1951

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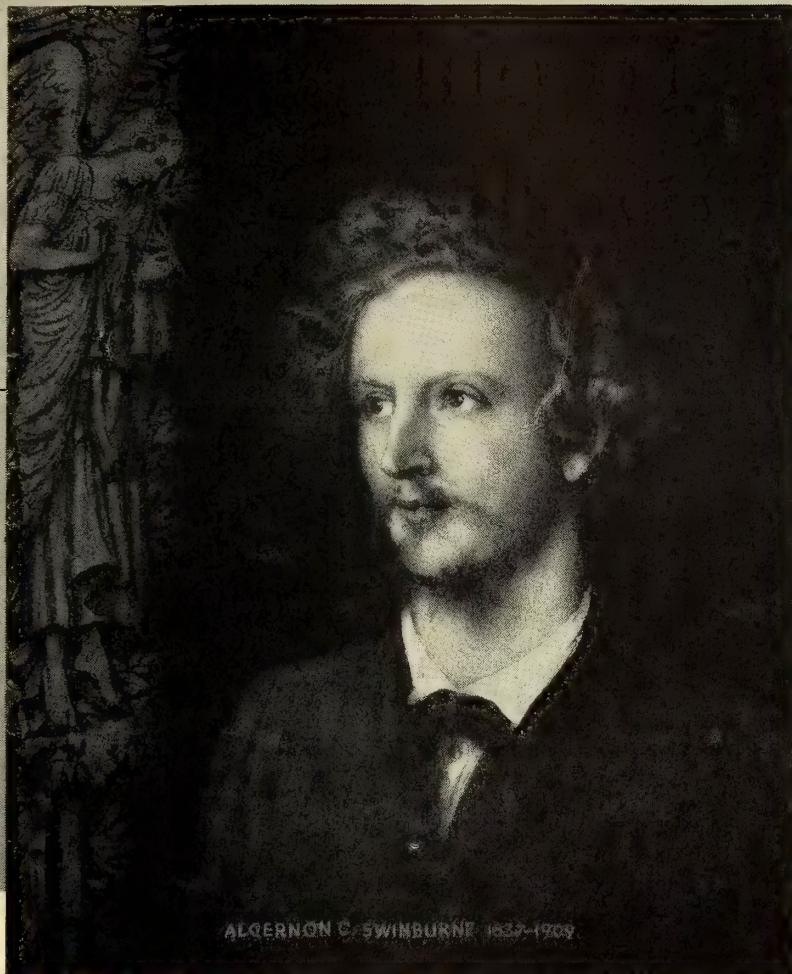


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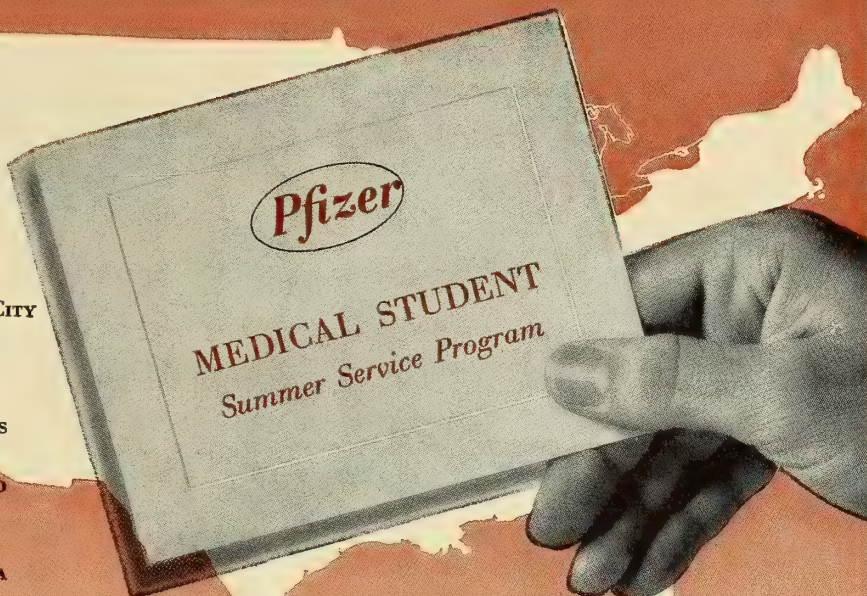
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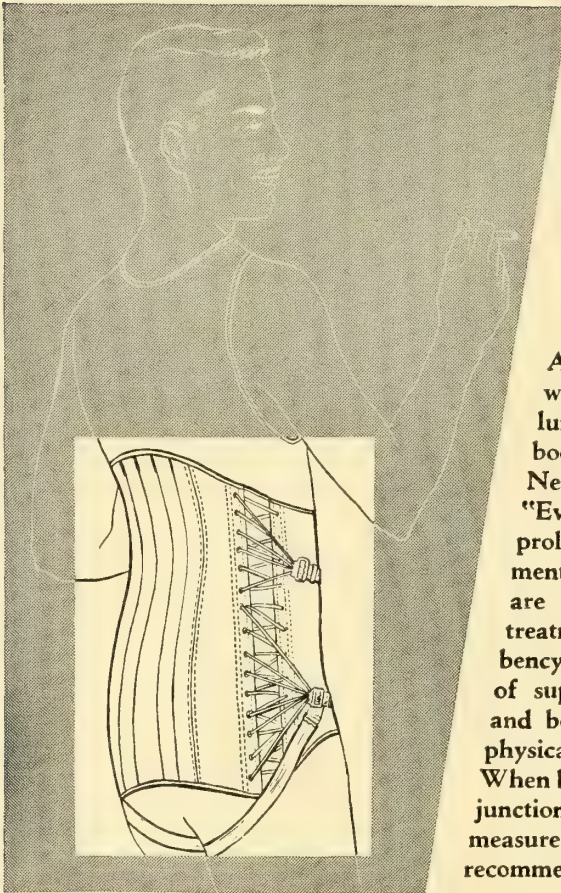
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Chapter XXXIX, Page 580

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1. Towse, R. C., Berberian, D. A., and Dennis, E. W.: *New York State Jour. Med.*, 50:2035, Sept., 1950.
2. Berberian, D. A., Dennis, E. W., and Pipkin, C. A.: *Am. Jour. Trop. Med.*, 30:613, Sept., 1950.



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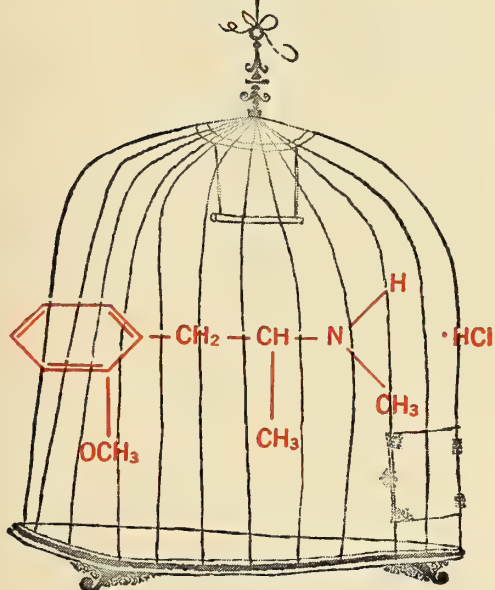
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ORIGINAL ARTICLES

MEDICAL FUNGI

The infections and the allergies that they provoke

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There are many fungi capable of provoking disease in the human. Some of these fungi are purely saprophytic and, therefore, are referred to as nonpathogenic but these fungi are capable of producing disease in man even though they do not invade the tissues of the host. Spores of many of the nonpathogenic fungi are capable of acting as antigenic substances in a manner similar to pollens, thereby initiating the clinical symptoms of allergic rhinitis and bronchial asthma. Other fungi are parasitic and are spoken of as pathogenic fungi because they invade and destroy tissue.

The very nature of the mycotic infection to proceed slowly at first and then become accelerated would suggest that the causative fungi at first rely on dead or injured tissue to grow, that they have slight inherent invasive power and that they are able to spread only after some change has taken place in themselves or in their environment. There has not been any evidence to date that they increase in virulence with the progress of the infection. It is reasonable to assume, therefore, that during the course of the mycotic infection the tissues of the host become altered. This alteration in the tissues of the host may be due to the liberation of toxins by the fungi or to the development of hypersensitivity on the part of the host to the fungi or their breakdown products.

There are 4 classes of fungi. These are the Basidiomycetes, the Ascomycetes, the Phycomycetes and the Fungi Imperfecti. The class,

Basidiomycetes, comprise in part the large, fleshy fungi with compact mycelium, for example the mushrooms and the puffballs. There are, however, more minute forms included in this class and these are the plant parasites, the smuts and the rusts. The Ascomycetes are the largest class of fungi, including many plant pathogens as well as molds that are important to the bacteriologist. This class of fungi is characterized by the fact that spores are formed in a membrane or sac called the ascus. There are usually 8 spores in an ascus. The Fungi Imperfecti possess the characteristic mycelium of Ascomycetes and produce spores similar to those formed by the Ascomycetes yet they do not form ascospores or at least ascospores have not been demonstrated. The Phycomycetes are the most primitive class of the fungi. They develop loose, non-septate mycelium presenting a cotton-wool appearance. Mucor and Rhizopus are common examples. The molds of interest to the bacteriologist and the clinician fall, for the most part, into the class of Fungi Imperfecti. The rusts and the smuts of the Basidiomycetes and Mucor and Rhizopus of the Phycomycetes are exceptions. The class, Fungi Imperfecti, is divided into 3 orders and one order, the Hyphomycetales, includes most of the molds of medical interest.

The Saprophytic Fungi as Excitants of Disease in Man

The spores of some saprophytic fungi just as the pollens of trees, grasses and weeds are capable of setting off allergic reactions in the respiratory passages with the subsequent manifestations of rhinitis and bronchial asthma. The

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spore content of the indoor and outdoor atmosphere varies somewhat in concentration and in character depending upon climatic conditions. The concentration of the mold content of indoor atmosphere is higher in damp, warm and humid localities than in dry and warm or in dry and cold areas. The concentration of molds in the outdoor atmosphere is higher in the agricultural areas during the growing season of vegetation than it is along the coastal areas. The fact that climatic conditions affect the atmospheric concentration of the mold spore content has lead many investigators in Holland, Spain, Denmark, Sweden and this country to incriminate molds as causes for "climatic asthma." The mold spore counts of outdoor atmosphere have been studied in many sections of the United States at regular intervals since 1933. Regardless of where the mold spore counts have been made there is a certain uniformity in regard to the genera that are most prevalent. *Penicillium*, *Aspergillus*, *Hormodendrum*, *Alternaria*, *Mucor* and *Rhizopus* predominate in this country as well as abroad. It is generally conceded that *Penicillium* and *Aspergillus* and sometimes *Mucor* predominate mostly indoors, while *Hormodendrum* and *Alternaria* predominate outdoors.

The potentiality of mold spores as excitants of inhalant hypersensitivity is actuated by their buoyancy. The average diameter of such spores ranges from 3 to 5 microns, whereas the diameter of common airborne pollens varies from 15 to 40 microns. *Alternaria* and *Hormodendrum* spores, originating in Southern Minnesota have moved with air masses as far East as New York City and as far South as Oklahoma City in a period of only 24 hours. Aviators have recovered plant disease spores at altitudes of 18,000 feet. Furthermore it has been demonstrated that the spores of *Hormodendrum* may be carried in large numbers throughout large buildings within a few minutes after they have been liberated in a single room and that these spore enter in large numbers all of the rooms of the building in which air itself has had free access. These data serve to impress upon us the potential ubiquity of molds and their spores.

Sixty-six valid special of the genus *Aspergillus* and over 600 species of the genus *Penicillium* have been described. There are only a few mycologists in this country who are qualified to attempt identification and classification of the species of these genera. It for this reason

that no attempt is made to differentiate species of *Aspergilli* or of *Penicillia* in the conducting of mold surveys.

Penicillia are characterized by the production of conidia from sterigmata which are produced in clusters or whirls known as verticils. Verticils come off of short branches called metulae. Depending upon whether there are one or more metulae and whether or not they are arranged symmetrically or asymmetrically the *Penicillia* are classified.

The word *Aspergillus* means a special type of brush used for the sprinkling of holy water and the name of the genus has derived its origin from the fact that the conidia (spores) are arranged so as to resemble the appearance of a brush. The conidiophore, or the spore bearing portion of the mycelium, is made up of a foot-cell which is simply an enlarged mycelial cell, the stalk, the swelling at the end or the vesicle and the chains of conidia. Between the vesicle and the conidia are little stalks known as sterigmata. The conidia arise from the sterigmata. In some species of this genus secondary sterigmata come off of the primary ones and in these species the conidia arise from the secondary sterigmata. Mycelium and conidia may be colored and the color offers assistance in identification. *Aspergillus* and *Penicillium* species are found on a variety of substrates. They are abundant on soil and dried vegetable matter, such as hay and grains. Unlike *Penicillium*, *Aspergillus* tolerates high temperatures. Because of the abundant number of species of these genera the routine skin testing with a few isolated species of *Aspergillus* or of *Penicillium* acquired from some drug manufacturer is a demonstration of ignorance and folly on the part of the skin tester. If hypersensitivity to molds is suspected a study of the patient's own atmosphere and a preparation of extracts from those molds in his atmosphere is essential.

Cladosporium and *Hormodendrum* were at one time considered as names for two different genera. The name *Hormodendrum* unfortunately predominates over *Cladosporium* in the medical literature, even though *Cladosporium* by reasons of priority is the correct name for the genus. A small, dark, olive-green, velvet colony of *Cladosporium* is familiar to anyone who has manifested even a meager interest in molds. These molds are found in the soil, decaying leaves, straw and other vegetation. They are

considered to be of some importance in the spoilage of malt and of stored tobacco. *Cladosporium herbarium* is a species of this genus which is most commonly isolated. *Cladosporium pulvum*, the tomato mold, has caused asthma in green house tomato growers.

Members of the genus *Alternaria* form dark, olive-green or brown colonies similar to those of *Cladosporium* except that the colonies are looser and more woolly in type. Molds of this genus are characterized by the large multi-chambered spores which occur in chains and sometimes have segments of mycelium between them. Species of this genus, as the species of *Cladosporium*, are common plant pathogens. It is undeniable that these molds occur in the greatest multitude throughout the agricultural regions of this country and particularly in such areas they may act as excitants of inhalant allergy.

Mucor and *Rhizopus* are the two genera of the *Phycomycetes* that are of particular interest to the clinician and the bacteriologist. Both molds fill up a petri dish with mycelium but *Rhizopus* covers the agar rapidly, climbs up the side of the dish and attaches itself to the under-surface of the lid by holdfasts which are also known as *Rhizoids*.

Rhizopus nigricans is by far the most common of all molds belonging to the class *Phycomycetes*. It is a common air contaminant and important in the spoilage of fruits, especially stored sweet potatoes. Strawberries are also susceptible and the fungus is responsible for the disease known as leak causing softening and dripping of the fruit.

There are many species of *Mucor*. They are frequently referred to as the bread molds and are found abundantly in the soil, in manure, in starchy food stuffs and on fruit. Along with the *Rhizopus* they give rise to loosely meshed aerial mycelia which may be grey or white in color.

The smuts and rusts belong to the class of *Basidiomycetes* and are plant parasites. Nearly everybody is familiar with the appearance of an ear of corn that has been affected with the corn smut, *Ustilago Leae*, and the disease of wheat known as black stem rust which is caused by the rust *Puccinia graminis*. Other grains are similarly affected by rusts and smuts and the spores of these plant parasites are capable of

producing allergic reactions in the respiratory passages.

There is the possibility that molds represent at least a part of the protein content of crude house dust and an attempt is being made by several workers in this country and abroad to determine the role of mold hypersensitivity in patients with so-called house dust sensitivity. The colossal amount of work and knowledge that is required to shed light upon the role of fungi as excitants of inhalant allergy is enough to dim the enthusiasm of even the most ardent of investigators, and it is perhaps for this reason that our understanding in its regard is still so very limited.

The Pathogenic Fungi

The pathogenic fungi are *Fungi Imperfecti* belonging to the order of *Hyphomycetales* and for the sake of clarity and convenience may be divided into two groups, that is those producing superficial infections and those producing deep-seated infections. The various superficial mycotic infections will be discussed together under the heading of "Dermatophytosis" and the deep seated mycotic infections will be taken up individually.

Dermatophytosis

Dermatophytosis is a more or less superficial infection of the skin, the hair and the nails caused by anyone of the fungi known as the dermatophytes. The fungi included in the genera of *Trichophyton*, *Epidermophyton*, *Microsporum* and *Candida* (*Monilia*) are referred to as dermatophytes. These parasites may infect many different body regions and have a wide range of morbid anatomical expressions. It is because of these two latter characteristics that so many confusing terms have invaded the literature. *Tinea* which means "worm" precedes *pedis*, *capitis* and *cruris* on occasions to denote the region of the body infected and then on other occasions is used before *circinata* and *imbricata* to describe an anatomical expression of the infection. Only one or two species of each of the genera referred to above are of clinical importance. *Trichophyton mentagraphytes* and *Trichophyton rubrum* commonly infect the skin and the nails of the feet. *Epidermophyton floccosum* commonly infects the skin of the groin. *Microsporum audouini* and *Microsporum canis* commonly infect the hairs of the scalp in children. *Candida albicans* which may also produce deep seated lesions commonly infects the

mucus membranes of the mouth (thrush) and the vagina.

Diagnosis. The matter of making a clinical diagnosis of dermatophytosis is ordinarily not difficult. Occasionally chemical dermatitis and contact dermatitis simulate dermatophytosis. Furthermore, bacteria may produce lesions on the feet similar in characteristics to those produced by the fungi. Therefore, because the diagnosis of fungous infection cannot be made with certainty in all cases on clinical grounds alone, the laboratory evidence of the presence of a dermatophyte by microscopic examination or by culture is essential in a scientific study of a skin affection where dermatophytosis is suspected. The dermatophytes are present in the skin and in the hair as continuous or fragmented hyphae. The demonstration of hyphae by microscopic examination of material from the infected areas is sufficient to make a diagnosis of dermatophytosis. On Sabouraud's agar the dermatophytes produce a characteristic sporulating mycelium.

The material to be studied must be collected properly. A scalpel should be used to obtain scrapings of skin from lesions on the toes and in the groin. The active edge and not the center of the lesion should be scraped because fungous infections heal from the center and if the hyphae are to be found they will be located in the periphery of the lesion. If the lesion is vesicular the roof of the vesicle should be completely removed with scissors and if the hair is affected an affected hair should be epilated with forceps. The specimen for examination should then be placed on a slide and covered with 10 per cent sodium hydroxide. Several hours must elapse to allow the sodium hydroxide to clear the specimen before making the microscopic examination.

It is desirable also to culture material from infected areas. Skin scrapings, or the roof of a vesicle, or an infected hair should be planted on Sabouraud's agar and incubated at 30 degrees C. The identification of the fungus by its growth and microscopic cultural characteristics should be attempted only by an experienced mycologist. The isolation and classification of the fungus is an academic nicety but is not essential for the proper treatment of the patient.

It is important to discuss the value of skin tests in diagnosing dermatophytosis. Once the

body has become infected by a fungus certain alternations occur which affect the reactivity by the tissues toward subsequent contact with the fungus or the protein of the fungus. This altered reactivity that results from infection is spoken of as "bacterial hypersensitivity", "hypersensitivity of infection", or "tuberculin type hypersensitivity". It is quite possible that an anaphylactic type of hypersensitivity to the fungus or fractions of the fungus may also develop.

Trichophytin as it is made available on the commercial market has very limited assets. To perform the test 0.1cc of a 1-30 dilution of Trichophytin (Lederle) is injected intradermally and interpreted in the same manner as a tuberculin test. A positive test only indicates that at some time in the immediate or distant past the host has been infected with one or more of the Trichophyton fungi. A negative test is of some help in ruling out the presence of an infection with the Trichophyton fungi but it must be remembered that the fungi vary in their ability to sensitize and that fungous infection without skin sensitivity to Trichophytin is possible. Then, too, the infecting organism may not produce antibodies that will react with the commercial Trichophytin, that is, there may be a lack of specificity due to the genus and the species of the infecting organism. Although the immediate whealing reaction to Trichophytin has been observed and does definitely occur there has been little thought of its significance. The immediate reaction can be assumed to be an indication of the presence of anaphylactic hypersensitivity and it may be that the development on the part of the host of anaphylactic hypersensitivity explains its aptitude to develop concomitantly with the fungous infection such clinical manifestations of anaphylactic hypersensitivity as urticaria, purpura, migrating phlebitis, erythema nodosum and papular and eczematoid eruptions. Any of these various eruptions may or may not occur with dermatophytosis and are usually spoken of as trichophytids.

The Trichophyton fungi play a role in the development of "spontaneous" allergic manifestations to penicillin. It has been fully demonstrated that several strains of Trichophyton mentagrophytes elaborate antibacterial substances similar in some respects to penicillin. This fact may or may not be of significance in explaining these "spontaneous" allergic eruptions to peni-

cillin because there is increasing evidence that previous occurrence of fungous disease accounts for this type of penicillin sensitivity. The skin reaction to the intradermal administration of penicillin (2,000 units) in these individuals resembles in time of development and appearance a Trichophyton reaction and this delayed reaction to the cutaneous test with penicillin is of practical importance as an aid in the diagnosis of the "spontaneous" type of reaction. The clinical manifestations of this spontaneous sensitivity to penicillin characterized by an erythematopapulovesicular eruption which tends to localize first on the hands, the feet and in the groin and then spread over the body, must not be confused with the serum-sickness type of reaction which is induced by treatment with penicillin.

Odiomycin is a broth filtrate of *Candida albicans*. As it has been made available to the medical profession it has no value in the diagnosis of infections due to *Candida albicans*. The term Odiomycin is as inexact as the material which bears the name. The microorganisms that are now rightfully classed in the genus, *Candida*, have been referred to as belonging to the genera of *Oidium* and *Monilia*. Such clinical manifestations of anaphylactic hypersensitivity as eczematoid dermatitis and bronchial asthma may develop during an infection from *Candida albicans*. Certain cases of miliaria are thought to be a hypersensitive manifestation of infection from *Candida albicans*. In the instance of miliaria and eczematoid dermatitis, the focus of infection has been described to be intestinal. A case of bronchial asthma that was recently reported followed a bronchial infection with *Candida albicans*.

The fact that hairs infected by *Microsporum* dermatophytes fluoresce under filtered ultraviolet radiation is frequently used as an aid in the diagnosis of fungous infections of the scalp in children. Inexpensive units for the production of filtered ultraviolet radiation are available on the commercial market. These units are commonly referred to as "Wood's lights", being named for their inventor, Dr. Robert Wood, Emeritus Professor of Physics at the Johns Hopkins University.

Treatment. A compound to be effective in the treatment of dermatophytosis must first possess the power to inhibit the growth of fungi or actually kill the fungi. Secondly, it must be able to penetrate the stratum corneum and

come into contact with the fragments of hyphae that are embedded there. Thirdly, the compound should possess as antibacterial effect because essentially every infection is complicated by secondary bacterial infection and the hypersensitive reaction to this bacterial infection. Fourthly, the compound and the vehicle in which it is placed should be neither irritating nor sensitizing.

As the result of investigations carried out during the last War two preparations which satisfy the above qualifications were developed. These preparations now generally familiar are made commercially available under the trade names of "Desenex" and "Sopronal". There is essentially no difference in the clinical effectiveness of these preparations and either preparation is satisfactory for the treatment of dermatophytosis of the feet, the groin and the smooth skin and is an improvement over any one method of treatment that has been formerly employed. In this respect the treatment of dermatophytosis has been fairly standardized. For the treatment of dermatophytosis of the feet either ointment should be applied over the toes, between the toes and under the toes every night. The following morning the ointment should be removed with soap and water or with a towel and the feet dusted with either "Desenex" or "Sopronal" powder. Some of the powder should be dusted into the shoes. Therapy must be continued until the lesions have completely healed and then continued for several weeks thereafter. It is important, furthermore, to stress that the use of keratolytic agents, the procedure of opening widely vesicular lesions on the soles of the feet and the use of warm potassium permanganate (1-3000) soaks for acute eczematoid lesions should not be lost sight of and must supplement the use of either "Sopronal" or "Desenex" therapy.

For the treatment of dermatophytosis of the groin or smooth skin either ointment should be applied every night and every morning. The ointment should also be applied on the normal skin immediately surrounding the infected area. The treatment must be continued for approximately one week after the lesions have completely healed.

To date the only completely satisfactory method of treating dermatophytosis of the hairs of the scalp has been x-ray epilation. This treatment must be administered by an expert.

The development of the fatty acids as inhibitors of pathogenic fungi promises also to lend assistance in the treatment of infections due to *Candida albicans* and their employment in the management of infections due to this organism will be discussed later under the heading *Candidiasis*.

Actinomycosis

Actinomycosis (Fig. 1) is the most common, the most readily recognized and the most widely distributed of the severe systemic mycoses. The term actinomycosis does not refer to one specific disease caused by one specific organism. The term does, however, indicate an infection due to an actinomycete.

In human infections 90 per cent are caused by the anaerobic *Actinomyces bovis*, while only 10 per cent are caused by the anaerobic *Nocardia* species. The course of the disease, the diagnosis and the treatment are essentially the same for both types of infection. The mode of infection and transmission has not been firmly established. It is commonly taught that the habit of chewing straw leads to infection but *Actinomyces bovis* has never been isolated from vegetation. On the other hand the organism is known to be commonly present in and about carious teeth, in dental scum and in crypts of tonsils and it is reasonable to assume that the infection disseminates from these areas. Located in such regions the organisms are in strategic positions to invade locally the jaw giving rise to cervical actinomycosis, to be aspirated into the lungs to initiate a pulmonary infection, and to be swallowed to infect the intestines and the abdominal organs.

Clinical manifestations of actinomycosis, therefore, fall into three categories, depending entirely upon the region of the body affected. The cervical-facial region is the most frequently involved comprising about 60 per cent of the cases. The thoracic and abdominal regions are involved next in frequency and comprise, together, about 40 per cent of the cases. The cervical-facial type of infection usually remains localized and responds very favorably to treatment. In the thoracic and abdominal types of infection the prognosis is not so favorable.

Pulmonary infections with actinomycetes are usually bilateral and basal, but they may occur as a unilateral lesion in any part of the lung. Sometimes the infection may begin in one or more ribs and invade from there the lung and

the subcutaneous tissue. From the lung the infection usually extends to the pleura producing pleural pain and occasionally pleural effusion, but more frequently the fungus invades directly through the pleura to the chest wall giving rise to numerous draining sinuses. As the disease progresses the patient becomes anemic; there is a leucocytosis; the sedimentation rate is increased; there is a spiking type of temperature; and the patient presents numerable signs of a severe pulmonary disease. Dysphasia may occur from an extension of the infection into the mediastinum.

In the abdominal type of actinomycosis the primary lesion is often in the appendix and in all cases there are draining sinuses. At autopsy abscesses are frequently found in the liver.

The diagnosis is established by finding in sputa or pus the organism in the form of very characteristic "sulfur granules". These granules vary in size, have a radiating lobulated structure and are usually yellow in color. They are best observed with a low power microscope lens, but occasionally are large enough to be identified with the naked eye or with a hand lens. The interior of the granule does not stand out sharply but the clubs of the periphery are very refractile and appear as irregular lines marking the borders of the lobules. By crushing the granule between two slides and then staining with Gram's stain the Gram positive branched filaments can be demonstrated. These branched filaments make up the interior of the "sulfur granule". The *Nocardia* species do not commonly produce granules and because the small filaments are frequently acid-fast there may be difficulty in differentiating the stained organism from the tubercle bacillus. In contrast to the tubercle bacillus, treatment with sodium hydroxide kills the acid-fast actinomycetes. This fact is of practical importance in differentiating actinomycosis due to an acid-fast actinomycete and tuberculosis because guinea pigs fail to develop lesions following the injection of sputum containing acid-fast actinomycetes which has been treated with sodium hydroxide.

Actinomyces bovis is difficult to culture. Pus or sputum should be washed several times with sterile normal salt solution. Suspected granules should be recovered with a bacteriological loop, washed again in sterile normal salt solution and then placed in Brewer's media and incubated at 37°C. The colonies that gradually develop

appear as fluffy masses of mycelium suspended in the media. In addition to inoculating anaerobic media for the isolation of *Actinomyces bovis* a veal infusion agar containing 1 per cent glucose should be inoculated in an attempt to recover the anaerobically growing *Nocardia* organism. This species of actinomycete is not so difficult to isolate and will grow rather quickly on this media.

The treatment of actinomycotic infections is not altogether satisfactory. There are now numerous clinical notes in the literature proclaiming the effectiveness of sulfonamides and penicillin. In the majority of these reported cases, surgical measures, intensive iodide therapy and x-ray therapy supported the penicillin and sulfonamide therapy so that it is impossible to ascribe the entire clinical improvement of many of these reported cases to the action of either of the antibacterial drugs. More recently aureomycin has been reported to be effective in the management of actinomycosis due to *Actinomyces bovis* and just recently we have treated in the same manner with encouraging results a patient with actinomycosis due to *Nocardia asteroides*. Dr. Milton Huppert tested the sensitivity of the organism against various sulfonamides, streptomycin, dihydro-streptomycin, chloromycetin, penicillin, bacitracin, sodium iodide and aureomycin. Dr. Huppert clearly demonstrated that the organism was sufficiently sensitive to aureomycin to merit treatment with this antibiotic substance. A clinical report by Dr. Huppert and myself pertaining to these studies will soon be forthcoming in the medical literature. It must be concluded, therefore, that necessary surgical intervention, adequate x-ray therapy and intensive iodide administration are usually essential adjuncts to sulfonamide, penicillin and aureomycin therapy if optimal results are to be obtained in the treatment of this serious chronic mycotic infection.

Coccidioidomycosis

Coccidioidomycosis (Fig. 2) caused by *Coccidioides immitis*, produces two different clinical types of infection. The primary form of the disease, which is an acute but benign self-limiting respiratory disease, occurs by the tens of thousands in the arid regions of the Southwestern portion of the United States. It has been demonstrated that coccidioidomycosis is an endemic disease of rodents in the arid regions of the Southwest; that the organism is present

in the dust and soil of these areas; and that it gains entrance into the human body by dust particles through the respiratory tract, or more infrequently into the skin following injury to the skin. Quite often individuals living in the endemic area become infected without manifesting any clinical evidence of the disease. Furthermore, the lesions heal and confer upon such individuals immunity against subsequent infection.

The symptoms of primary pulmonary coccidioidomycosis resemble the signs and symptoms characteristic of many acute but mild respiratory infections. There is usually fever accompanied by a cough with pains in the chest, chills and sore throat. The sputum is scanty and rarely contains blood. The incubation period varies from 1 to 3 weeks. The physical findings referable to the lungs are usually not very revealing, but occasionally there may be some change in the breath sounds. Eight to 14 days following the onset of the infection hypersensitive reactions, such as erythema nodosum, erythema multiforme and arthralgia may occur. Roentgenograms of the lungs during the primary infection may reveal fan shaped densities extending out from the enlarged hilar nodes. There may or may not be definite parenchymal lesions. At times soft infiltrations occur throughout the lungs. Pulmonary cavities are not common during the first stage of the disease but when they do occur they may persist for a period of years without any deleterious effect to the patient.

Approximately one per cent of the primary cases develop into the progressive form of coccidioidomycosis, which is a chronic malignant disseminated disease involving the cutaneous, subcutaneous, visceral and bony tissues. The symptomatology of the progressive infection depends entirely upon the site to which the fungus has migrated. If the lung infiltrations persist for a period of more than 6 weeks a progressive form of the disease should be suspected. The pulmonary infiltrations increase in amount and there is enlargement of the mediastinal glands. Cavities may enlarge and the sputum becomes muco-purulent and occasionally tinged with blood.

If the progressive form of the disease is suspected the entire skeleton should be x-rayed. Typical lesions in the bones appear as sharply circumscribed areas of destruction with scarcely

any reaction in the surrounding bone. Although any bone in the body may become involved the ribs, the vertebrae, small bones of the hands and the tibia are most frequently invaded in the order named. Dissemination also affects the joints and involvement of the ankle joint for an unknown reason frequently occurs. The wrists and the elbow joints are next most commonly involved in the order enumerated. In white patients meningitis is quite frequent and the course simulates that of tuberculous meningitis. In the dark skin races there is more of a tendency to the development of subcutaneous and joint abscesses.

Laboratory studies are helpful in making a diagnosis of coccidioidomycosis. In the primary form of the disease the sedimentation rate is increased; there is an increase in the percentage of circulating eosinophils; there is frequently a leucocytosis; and the skin test with coccidioidin is usually positive. Precipitins and complement-fixing antibodies are negative in mild cases of the primary form, but become positive in the severe infections. As recovery becomes manifest the precipitin and complement-fixing antibodies disappear. In the progressive form of the disease the skin test with coccidioidin is usually positive but becomes negative in the terminal phase of the disease. The precipitins and complement-fixing antibodies are present in high titers.

The organism, *Coccidioides immitis*, exhibits marked dimorphism. It grows on agar as a white cotton mold which pigments with age. Old cultures contain myriads of very large, thick walled arthrospores spoken of commonly as chlamydospores. These spores which are particularly adapted for maintaining vitality through long period of dormancy are considered to be the infective form of the fungus occurring in nature. When these spores are injected into animals they become spherical and enlarged. These large spherical cells commonly referred to as "spherules" gives rise to endospores by cleavage of their cytoplasm. The endospores escape when the wall of the "spherule" ruptures to repeat the parasitic phase of the life cycle. It is the "spherule" that is found in the sputum of the patient infected with *Coccidioides immitis*.

There is no specific form of treatment for coccidioidomycosis. A strict regime of bed rest is the best method of effecting a cure. In other

words, the patient should be treated as though he had tuberculosis and should remain in bed until he has clinically recovered; until the x-rays have revealed the lesions to be regressing; and until the sedimentation rate has returned to normal.

The prognosis in the primary form of the disease is excellent but in the progressive form is very grave. The mortality rate is given as 60 per cent, but it is probably much higher as the primary benign type of the disease was not differentiated from the severe progressive form of the disease in the early reports of the literature.

Blastomycosis

Blastomycosis (Fig. 3) is a relatively common mycotic disease, characterized by the formation of granulomatous lesions in various parts of the body, but with a marked predilection for involvement of the skin, lungs and bones. Blastomycosis occurs with the greatest frequency in the Mississippi Valley, across Tennessee into North Carolina and down into the Southeastern States. Dr. T. C. Gilchrist, a dermatologist of Baltimore, first described the disease and later named the causative fungus, *Blastomyces dermatitidis*. The fact that Dr. Gilchrist was primarily interested in cutaneous medicine is manifested by the appendage which he coined for the genus *Blastomyces*. Actually the name Blastomycosis is doubly a misnomer. It was first thought that the causative organism was a true yeast and secondly that *Blastomyces* was the proper scientific name for the yeasts. However, the organism is not a true yeast and *Saccharomyces* is the proper scientific name for the yeasts.

Blastomycosis is not spread from man to man but evidently is derived from some source in nature. Infections may occur in patients of any age but the disease does occur nine times as frequently in males as in females. The infection may begin primarily in the skin and remain localized for months or years before it spreads to the internal organs. In the majority of the cases the primary lesion appears on the skin of the face, the hands, the wrists or the forearms. There appears first a firm papule and about this a number of secondary nodules develop which gradually enlarge and coalesce. These lesions break down and discharge purulent material from their centers. As the lesion progresses there develops a large elevated mass of tissue with an irregular ulcerated surface

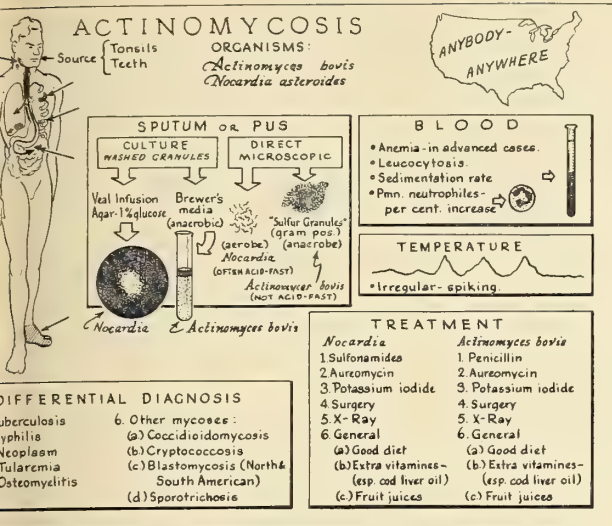


FIGURE 1

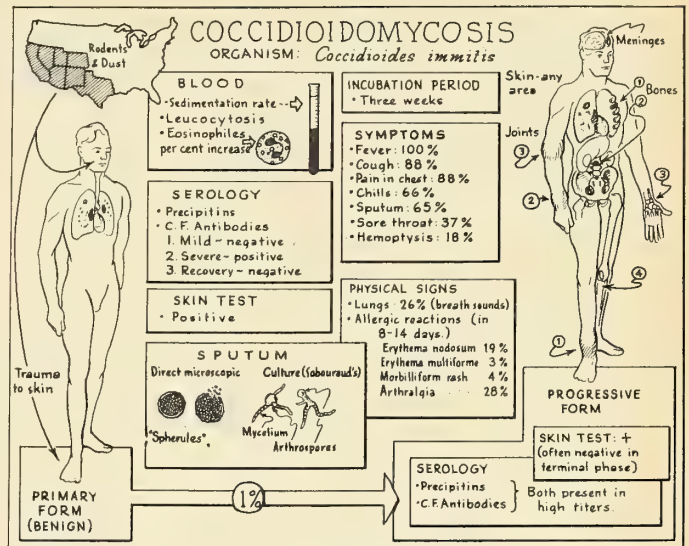


FIGURE 2

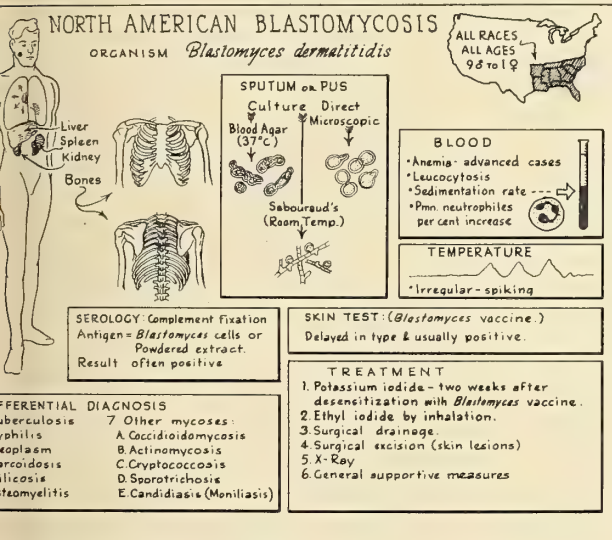


FIGURE 3

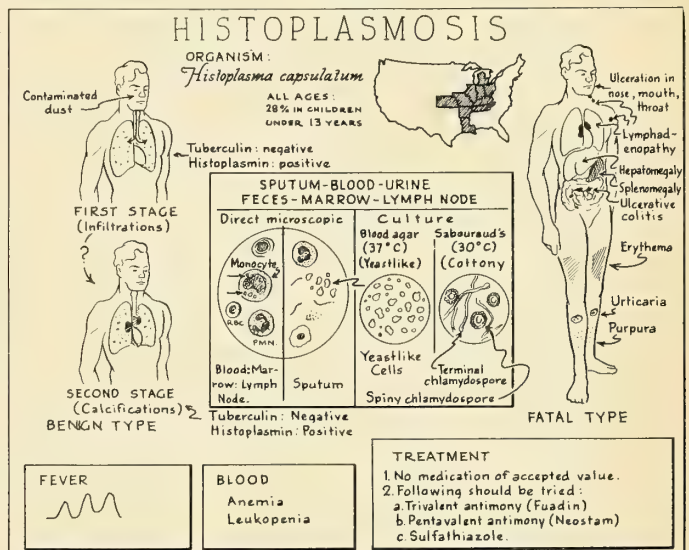


FIGURE 4

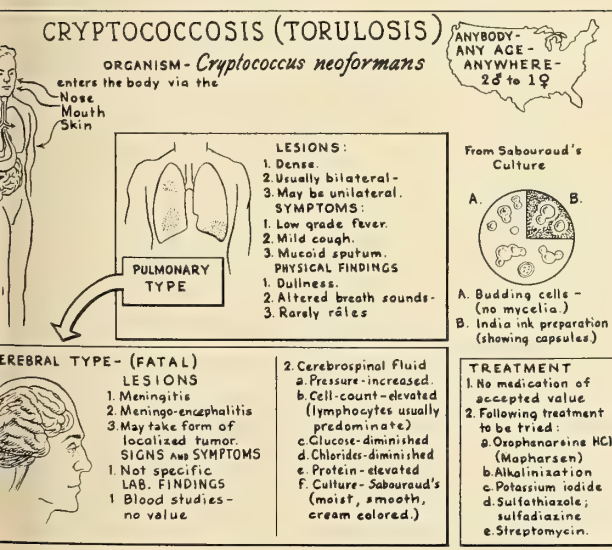


FIGURE 5

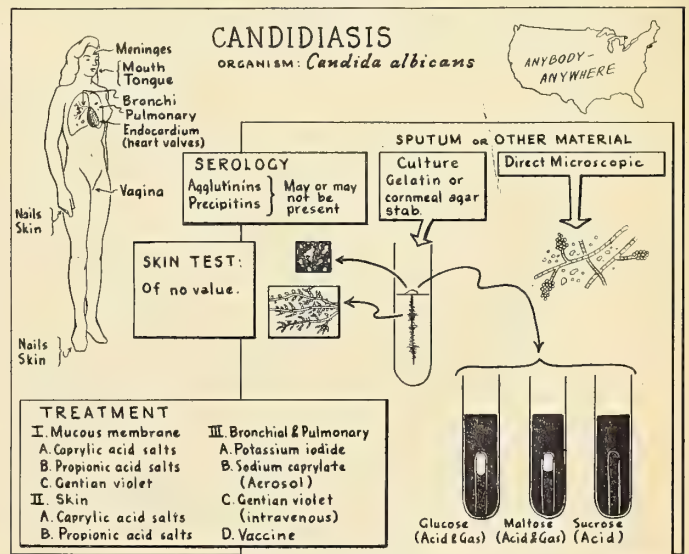


FIGURE 6

that resembles somewhat a tuberculous ulcer. Healing occurs first in the central portion of the lesion and is followed by the formation of scar tissue.

Most cases of systemic blastomycosis begin with pulmonary infection. The onset is rather insidious and the symptoms resemble those of an ordinary subacute respiratory tract infection with a dry cough, some pain in the chest, slight fever and mild shortness of breath. As the infection progresses the shortness of breath is accentuated, the fever becomes higher and there is loss of weight and strength. Roentgenograms of the lungs reveal enlargement of the mediastinal lymph nodes. Dense masses are often observed located near the hilum and project into the lung fields with irregular outlines. The observance of such a hilar mass may suggest a bronchogenic carcinoma. The mediastinum frequently becomes invaded in the latter stages of the disease with involvement of the pericardium and the heart. The infection may disseminate from the lungs by way of the blood stream and when disseminated blastomycosis is suspected x-rays should be taken of the entire skeleton. The ribs and the vertebrae are most frequently involved, and the latter may be destroyed resulting in collapse with compression of the spinal cord. It is difficult to differentiate the bony lesions of blastomycosis from those seen in coccidioidomycosis and actinomycosis. The abdominal viscera also become involved in the disseminated form of the disease with abscesses appearing in the liver, spleen and kidneys. As the disease progresses the sedimentation rate becomes increased and there is a hypochromic anemia and a leucocytosis with an increase in the percentage of polymorphonuclear leucocytes.

Skin tests with a vaccine prepared from the yeast phase of the organism are positive in most of the extensive skin cases and in all of the systemic cases. Serological tests are not always reliable. Complement-fixating antibodies are ordinarily present in the systemic cases but a negative complement-fixation test does not rule out the presence of the disease.

The diagnosis is established by demonstrating the organism in pus or sputum. In the body tissues the fungus occurs only as a round or oval yeast-like cell which reproduces by budding. These cells are easier to demonstrate if the material for examination is first treated with 20 per cent sodium hydroxide. The finding of

doubly contoured budding cells with granular contents and which in size are slightly smaller than leucocytes makes the diagnosis certain. Cultures should be made on both Sabouraud's and blood agar media. On Sabouraud's agar the colonies first appear smooth and greyish, but soon become wrinkled and finally a white cottony growth develops. Cultures on blood agar incubated at 37° C. do not develop a filamentous growth but remain yeast-like in appearance.

If the patient's infection is confined to the skin and if the lesion is small and readily accessible surgical removal of the lesion is advisable. If, however, the skin lesion is not suitable for surgical excision x-ray therapy in addition to large doses of potassium iodide should be recommended. In the patient with pulmonary blastomycosis, with or without dissemination, considerable care should be given to the plan of therapy. Administration of iodides to patients hypersensitive to blastomyces vaccine frequently causes an extension of the infection. Skin tests with blastomyces vaccine should be performed on every patient before iodides are administered. If the skin tests produce an area of erythema and induration 2 cm. or larger in diameter the concentration of the vaccine should be diluted a thousand or ten thousand times depending entirely on the degree of the skin reactivity. Desensitization treatment should be started with 0.1cc. of the diluted vaccine and this dose increased by 0.1cc. Treatment should be given 3 times weekly and finally when a dose of 1cc. has been reached the procedure should be repeated, beginning with a 0.1cc. of the next lowest dilution and so on until undiluted vaccine is administered. If local reactions to the vaccine should occur the dose should be reduced and the highest dose which just fails to produce a local reaction should then be maintained without further attempt to increase the dosage. Iodide therapy may be started after 3 weeks of desensitization treatment. The dosage of potassium iodide should be increased gradually. Five drops 3 times daily is a safe beginning dosage and this amount should be increased only 1 drop a day until a maximum of 20 drops 3 times daily has been given. This dose can be maintained. On the other hand if the patient fails to give a positive skin reaction to blastomyces vaccine or gives a reaction less than 1 cm. in diameter the iodides may be administered rapidly, the initial dose being 5 drops 3 times a day with an

increase of 3 drops each day until approximately a maximum dosage of 60 drops 3 times a day are given. If larger doses can be given this is advisable and it is wise to administer the largest dose which the patient can tolerate without signs and symptoms of iodidism. Sodium iodide intravenously, in doses of 1 gram once or twice daily, may be used to supplement the oral potassium iodide therapy. Ethyl iodide administered by inhalation is also frequently effective. In regard to this route of iodide administration it is suggested that 0.25cc. of ethyl iodide be inhaled 3 times daily. The dose may be increased by 0.25cc. every 3 to 4 days until the patient is taking as much as 1cc. 3 times daily. Inhalation therapy may be combined with the oral or the intravenous route of administration. Surgical drainage is indicated where there are large accumulations of pus. Here again better results are obtained in the hypersensitive patient if surgical drainage is deferred until desensitization therapy has been accomplished. X-ray therapy is a useful adjunct for the treatment of pulmonary blastomycosis. The doses should be smaller than those used for neoplasm of the lung and should be given while the patient is receiving iodides. X-ray therapy should not be given to the hypersensitive patient, however, until some degree of desensitization has been accomplished.

Histoplasmosis

The disease, histoplasmosis (Fig. 4), was first discovered in the Panama Canal Zone by Darling in 1906. Darling, originally believed the causative organism was a protozoan and, therefore, gave it the name *Histoplasma capsulatum* and accordingly named the disease histoplasmosis. It was not until 1934 that De Monbreum proved that the causative organism was a fungus. De Monbreum then proposed to change the name of the fungus and the name of the disease because of Darling's misconception, but since Darling created a new generic and a new specific name for the parasite such a change is not warranted. In 1939 De Monbreum suggested that a relatively mild and non-fatal form of the disease might exist which was similar in nature to the primary and non-fatal form of coccidioidomycosis. From that time to date there has been a certain amount of interest in this mycotic infection.

It was soon demonstrated that there was some association between histoplasmin sensitivity and

pulmonary calcification occurring in tuberculin negative reactors. Subsequent investigation conducted for the most part under the auspices of the United States Public Health Service indicated that the greatest number of individuals with positive histoplasmin tests resided in the states of Tennessee, Kentucky, Arkansas, Missouri, Indiana and parts of Ohio, Illinois, Kansas and Louisiana. It was only natural to postulate that these pulmonary calcifications in individuals with positive histoplasmin skin tests and negative tuberculin skin tests represented a primary benign form of the disease histoplasmosis. Studies in school children in Kansas City lent further evidence in the growing chain of knowledge that pulmonary infiltrations were distinguishable from tuberculous infiltration and probably represented the first stage of the benign type of infection, and that these infiltrations were the fore-runners of the pulmonary calcifications that had been noted previously. Furthermore, the strength of the circumstantial evidence was enhanced by the isolation of *Histoplasma capsulatum* from one of the Kansas City children possessing pulmonary infiltrations. The pathogenic process now has been followed from the negative roentgenogram of the lungs and negative histoplasmin skin reaction through the appearance of parenchymal infiltration with concomitant development of histoplasmin sensitivity to the final calcified foci in the lungs associated also with histoplasmin sensitivity.

The portal of entrance of the organism was purely speculative until 1949 when it was demonstrated that *Histoplasma capsulatum* was present in the soil and the rodents of the endemic area. It might then be postulated with some reservation that the organism enters the respiratory tract with dust particles in the manner identical to that of *Coccidioides immitis*. The fatal type of the disease presents a dissimilar picture from the benign primary type. At this time it is attempting to speculate in regard to the surprisingly few instances of progressive pulmonary histoplasmosis in view of the many cases of primary pulmonary infections. Perhaps the form of the organism which is inhaled is less virulent than the form which enters the body through the mouth and intestinal tract.

The clinical picture is usually that of emaciation, weakness, septic fever, anemia, leukopenia, splenomegalia and hepatomegalia. Occasionally there is ulcerative colitis and lymphadenopathy.

Manifestations of hypersensitivity such as erythema, urticaria and purpura may develop. Ulcerations in the nose, mouth and throat have been described.

The fungus in its parasitic phase is a small yeast-like organism ranging in diameter from 2 to 3 microns. These yeast-like bodies resemble closely the Leishman-Donovan bodies of kala-azar and invade the mononuclear cells in enormous numbers. Whenever the diagnosis of histoplasmosis is suspected the mononuclear cells of the circulating blood and the bone marrow should be examined carefully under an oil immersion lens for the intracellular bodies. If there is enlargement of the lymph glands a biopsy should be studied. In sputum the yeast-like bodies are extracellular. Cultures taken from blood, urine, feces, lymph nodes or sputum should be placed on both agar and Sabouraud's media. On Sabouraud's agar the organism produces a white cottony growth. Spores ranging in size from 10 to 25 microns are produced and from these spores rise finger-like projections 5 microns in length. The growth on blood agar is yeast-like. The organism, therefore, grows on Sabouraud's and blood agar media in a manner very similar to growth on the same media of *Blastomyces dermatitidis* and it is difficult to differentiate the two by their growth cultural characteristics. Further interest is lent to the problem with the realization that there are immunological cross reactions with blastomyces vaccine or blastomycin and histoplasmin. Furthermore, there is a geographical relationship between the organisms.

Adequate treatment for histoplasmosis has not been developed. Perhaps one of the reasons for this is that the diagnosis is rarely made before death. Trivalent antimony and pentavalent antimony should be given a trial. The organism in vitro has also been shown to be sensitive to sulfathiazole in a concentration of 50 mg. per cent. This laboratory observation should merit the trial of sulfathiazole in the treatment of histoplasmosis.

Cryptococcosis

Cryptococcosis (Fig. 5) caused by *Cryptococcus neoformans* (*Torula histolytica*) has a marked preference for the lungs, the brain and the meninges. In the American literature most of the instances of this disease will be found indexed under torulosis. The disease has been re-

ported from almost every country in the world. Although it may occur in all age groups males are involved twice as frequently as females. The organism gains entrance into the body through the nose, the mouth and lacerated skin.

The symptoms of primary pulmonary infection are neither specific nor diagnostic. The clinical picture is that of a subacute respiratory infection with a low grade fever and a mild cough. A small amount of mucoid sputum is produced which is rarely blood stained. The lesions in the lungs are often dense, resembling a massive tuberculous lesion or a neoplasm. They may develop in any part of the lung and they are frequently bilateral but may be unilateral or confined to one lobe. The physical findings suggest a lobar consolidation. It must be remembered that there is nothing characteristic about the pulmonary symptoms or signs or roentgenograms of patients with cryptococcosis.

The patient is usually and apparently recovering from the pulmonary infection when there is a spread to the brain or meninges precipitating the cerebral type of the disease. The symptoms of cerebral involvement are not characteristic. They may be those of a meningitis or meningo-encephalitis or they may take the form of a localized tumor. Examination of the cerebrospinal fluid usually reveals the pressure to be increased and the cell count to be elevated. Lymphocytes ordinarily predominate. Chemical studies on the cerebrospinal fluid reveal the glucose and the chlorides diminished and the protein elevated. Diagnosis is established by demonstrating the capsulated budding yeast cells in the centrifuged spinal fluid sediment. On Sabouraud's agar the organism grows slowly. At first the growth is moist, smooth and cream colored. As the culture ages the color changes to yellow and then to brown. A portion of the culture examined microscopically and in an India ink preparation reveals best the wide typical capsules. This capsule takes on a reddish color when the cells are stained by Gram's technique.

No effective method of treating this fungous infection has been reported. The disease is slowly progressive and usually fatal. The organism produces acid and it is for this reason that alkalization therapy has been suggested. Oxyphenylarsine hydrochloride (mapharsen), potassium iodide, sulfathiazole, sulfadiazine and streptomycin have all been tried but their specific effectiveness still remains in doubt.

Candidiasis

Of the many species included in the genus *Candida* only one, *Candida albicans*, is commonly pathogenic for man. The clinical manifestations of infections produced by this organism vary greatly and are dependent upon the region of the body affected. Candidiasis (Fig. 6), therefore, is a term which may designate an acute or chronic infection produced by the *Candida* organism occurring in the mouth, vagina, skin, nails, bronchi, lungs and infrequently in the endocardium and the meninges. It is important to call to the attention of physicians that mycologists have replaced the familiar name *Monilia* by the name *Candida*. The name of the fungus, *Monilia albicans*, therefore, becomes *Candida albicans* and the term moniliasis should be replaced by candidiasis.

The clinical manifestations of infections due to *Candida albicans* may be grouped as superficial and systemic. By superficial infections we are concerned with involvement of the nails and tissues about the nails; the skin, particularly of the axillae, the inframammary folds, the groin, the umbilicus, the interstitial webs of the feet and hands and the intergluteal folds; the mucus membranes, especially the mouth, and the vagina. There apparently is one predisposing factor that is common and necessary for the establishment of a superficial infection from this organism and that is moisture. In this regard a large portion of the patients with cutaneous candidiasis are obese. Diffuse sweating is often followed by infections with *Candida albicans*. Housewives, bartenders, waiters and bakers appear to be more prone to the infection because of their occupations. *Candida* infections occur rather commonly in patients with diabetes, probably because of the altered carbohydrate metabolism which favors the growth of the organism.

Clinical manifestations of anaphylactic hypersensitivity may develop during the course of infection. Eczematoid dermatitis of the face and certain cases of miliaria are thought to be clinical signs of hypersensitivity to *Candida* infections. In the instance of miliaria and facial dermatitis the focus of infection has been considered to be intestinal. Vesicular lesions on the hands have characteristics similar to a trichophytid and are considered to be manifestations of hypersensitivity.

Bronchopulmonary candidiasis is the term used to designate that type of *Candida* infection

in the lungs where the disease is confined to the bronchial tree. The term pulmonary candidiasis is reserved for infections involving the parenchyma of the lungs. Bronchopulmonary candidiasis, manifested by the signs and symptoms of an ordinary bronchitis, is not at all an uncommon infection. The temperature may be normal or only slightly elevated and the health of the patient is not seriously affected. The infection may disappear spontaneously or become chronic and mimic the symptoms of a chronic bronchitis of bacterial origin. Pulmonary candidiasis is not as common as the bronchial form but is a more severe disease. The areas of infection resemble those of a bronchopneumonia and are scattered throughout two or more lobes. Occasionally there may be lobar involvement. Rarely the meninges and the endocardium of the heart valves may become involved. Agglutinins and precipitins are not present in the sera of patients with superficial infections, but are present occasionally in patients with severe forms of the systemic infections. Skin tests are of no value in the diagnosis of candidiasis.

To establish the diagnosis of candidiasis one should find the budding organism by direct examination of sputum or exudates and isolate it in pure culture form on Sabouraud's media. Occasionally mycelia will be found in sputum or various exudates. On Sabouraud's media the organism grows as a yeast but when a stab culture is made in gelatin or corn meal agar the mycelial form of the organism is reproduced. To be absolutely certain that the organism obtained is the pathogenic species of *Candida* the organism should be tested for its fermentation reactions. It will form acid and gas in glucose, acid and gas in maltose, but only acid in sucrose media.

Sodium salts of various short chain fatty acids have been found to be fungistatic and fungicidal in different degrees for various pathogenic fungi when tested by in vitro methods. One of these fatty acid salts, sodium caprylate, is particularly effective against *Candida albicans*. Caprylic acid salts prepared in solutions, salves and suppositories are effective in the treatment respectively of thrush, cutaneous infections and vaginal infections produced by this organism. Salts of propionic acid have also been employed. The combinations of the two fatty acids are available commercially for the use in the treatment of this disease.

Sodium caprylate by aerosol has recently been described as a fairly effective measure in the treatment of bronchopulmonary candidiasis. Gentian violet administered intravenously has been recommended by some investigators for the treatment of pulmonary candidiasis. The dose is 5 milligrams per kilogram of body weight and may be repeated daily or every other day for 3 to 7 doses. Potassium iodide orally in doses to a point of intolerance is advised as an adjunct to treatment with either sodium caprylate or gentian violet. It is usually advisable before administering potassium iodide to give the patient 3 to 4 weeks of specific desensitization treatment with *Candida albicans* vaccine. The dilution and dosage employed are calculated in the manner described in the section on blastomycosis. The prolonged use of a *Candida albicans* vaccine in the management of patients with chronic infections is worthy of a clinical trial.

Sporotrichosis

Sporotrichosis was first discovered in Baltimore by Dr. B. R. Schenck in 1896. The causative fungus was named *Sporotrichum Schencki* 4 years thereafter. It is believed that the fungus grows on vegetation and that humans are infected from this source. Many cases have followed wounds of the upper extremities by thorns, straw and grains. Accidental laboratory infections have occurred and there is on record a case in which there was direct transmission from human to human.

The clinical picture of a typical case is so striking that once seen the disease will always be readily recognized. Extending from the primary lesion, which is usually an ulcer or abscess about the wrist, there will be seen upon the surface of the extremity a line of hard or soft elevated nodules that are neither hot nor tender. Between these nodules there are usually reddened lines that demarcate the course of the lymphatic vessels. If sufficient time has elapsed between the onset of the disease and the time when the patient first presents himself for treatment some of the softer nodules will have developed a draining sinus from which pus can be expressed. It is not usual for the disease to spread beyond the regional lymph glands, but there is a rare case reported in the literature from which metastatic lesions have occurred in the lungs, the liver and the testicles. Quite often the patient with sporotrichosis suffers from some

debilitating disease which lowers his resistance to infection sufficiently to allow the fungus to gain a foot-hold.

The diagnosis is established by culturing the organism from a subcutaneous abscess. A high percentage of positive cultures will be obtained if the material to be cultured is aspirated from an abscess that has not as yet opened. It is difficult to identify the organism microscopically from smears of pus. The character of the growth of *Sporotrichum Schencki* on Sabouraud's agar is distinctive. At first the colony is whitish, shiny and moist, resembling a bacterial growth, but as the age of the culture increases the whitish culture changes to a light tan, then to a coffee brown and finally becomes black. The surface of the colony usually remains shiny but becomes wrinkled with age.

There is less need of a diagnostic skin test for sporotrichosis than for other systemic fungous infections. This is because the clinical picture of the infection is so typical. A 1-100 dilution of a broth filtrate recovered after 2 weeks of growth possesses sufficient specific antigenic substance to elicit a positive tuberculin-like skin reaction in a patient infected with *Sporotrichum Schencki*. Polysaccharides derived from either the fungous mat or the broth filtrate are also effective for skin testing.

The disease responds dramatically to the administration of potassium iodide. Large doses should be given and it is preferable to administer the drug to the point of intolerance and maintain this dose until the patient has fully recovered.

Aspergillosis, Penicillois and Mucormycosis

In another section of this paper the species of *Aspergillus*, *Penicillium* and *Mucor* have been discussed and their importance in the production of disease has been related. Rarely they act as parasites and on such occasions act as the primary cause of disease in the external ear, nasal sinuses, bronchi and lungs, and even at times in the bones and meninges. Many cases of aspergillosis of the lungs have been reported from France, occurring particularly in individuals exposed to massive doses of fungus spores, such as squab feeders who take grain into their mouths to moisten it, fur cleaners who use rye flour, and agricultural workers exposed to the dust from thrashers. A few cases of pulmonary infection from *penicillium* and *mucor* species

have been reported. It must be remembered that various species of these organisms are frequently found in the sputa of patients with chronic bronchitis and infective bronchial asthma. In most instances they are accidental contaminants or at most only secondary invaders.

The primary infections from aspergillus, penicillium and mucor are rare and difficult to diagnose before autopsy. The symptoms are similar to those of other mycotic infections in the lung and to pulmonary tuberculosis. The diagnosis of bronchial or pulmonary aspergillosis, penicilliosis and mucormycosis cannot be made without

repeated demonstrations of branching hyphae in the sputum. Cultivation of the fungus is not enough. Prognosis is good in the mild cases, but is poor when there is massive involvement of the lung with or without abscess formation. Potassium iodide should be administered by either the slow or the rapid technique, depending upon the degree of hypersensitivity of the patient to his own organism. If there is evidence of hypersensitivity the patient should be desensitized before the administration of iodides according to the technique outlined in the section on blastomycosis.

THE CLINICAL APPLICATION OF CORTISONE AND ACTH IN ARTHRITIS AND RELATED CONDITIONS: METHODS AND PROBLEMS

Part I: METHODS AND CLINICAL OBSERVATIONS

By

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INTRODUCTION

This report presents our observations during a period of a little over one year in the use of cortisone and ACTH* in a group of 140 cases of arthritis and related musculoskeletal disorders. These consisted of 72 cases of rheumatoid arthritis, 27 of rheumatoid-like diseases and 41 patients with non-rheumatoid musculoskeletal conditions. During our comparatively short period of investigation we have endeavored to find the answer to certain questions regarding these new compounds. They are:

1. May they be employed as practical therapeutic agents?
2. What are the nature and frequency of undesirable side-effects and complications in the use of cortisone and ACTH, and how may they be avoided?

3. What are the hazards of prolonged administration of these substances?

We recognize that a study of such duration is insufficient for an adequate answer to all of these questions. We hope, nevertheless, that our experience to date may be of some value as an interim report in the rapidly growing literature on this subject, since the original historic announcements of Hench, Kendall, Slocumb and Polley. (1)

The removal of restrictions on the use of cortisone and ACTH and their availability demand a realistic approach to the problems created by their widespread administration. We are attempting, therefore, to summarize our observations on the effects of these compounds together with the procedures we have utilized to permit us to apply them as judiciously as possible in the present state of our knowledge. Included in our presentation are tables of those routines and methods which, it is hoped, afford greater

*ACTH supplied in part by Dr. John R. Mote, Medical Director, Armour Laboratories.

Cortisone provided in part by Dr. James M. Carlisle, Medical Director, Merck and Co.

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safety in the clinical administration of cortisone and ACTH. The basis for most of these procedures adopted by us and others undoubtedly will become clearer in the course of our discussion. (2-6)

METHODS OF ADMINISTRATION AND DOSAGE

All patients in our series were hospitalized for an initial period of study and administration of ACTH or cortisone. Preliminary to their use, base-line observations were carried out. After the compounds were started, the patients continued their usual rest, activity and analgesics until they themselves requested a change.

The routine followed in the administration of ACTH and cortisone is divided into two periods:

I. *Period of Initial Observation (2-3 weeks)*

1. a.) Daily or alternate days

Physical examination, especially for
Weight
Blood pressure
Skin and Mucosae
Emotional reactions and moods
Edema
Effects on coincidental disease

b.) Regulation of dosage

2. LABORATORY AIDS

INITIAL BASE-LINE TESTS (Essentials underlined)

Routine Urinalysis

Complete Blood Count

Sedimentation Rate

Blood:

Glucose, Urea Nitrogen, Uric Acid
Carbon Dioxide Combining Power,
(Potassium, Sodium, Chloride,
Cholesterol and Fractions, Calcium,
Phosphorus and Alkaline Phosphatase)

Electrocardiograms

Chest Plate

X-ray films of joints chiefly affected
(Lumbosacral Spine, lateral, in patients
over 50 years)

3. DIET AND SUPPLEMENTARY MEDICATION (during therapy)

Low sodium (and low carbohydrate in obese)

Potassium chloride (enteric tablets, Gm. 0.5, 2 p.c.)

Other medications—sedation for insomnia; analgesic complements during maintenance.

Instruction as to rest, exercise and physiotherapy.

II. PERIOD OF MAINTENANCE

1. Weekly Check-up, then q. 2-3 weeks, with complete observations.

2. Adjustment of dosage to attain rest periods, a few days or weeks (?)

3. Doses q. 2-3 days or daily (oral), lowest optimum amount; (ACTH actually required in 1-2 daily injections)

4. Laboratory studies during treatment
Fractional urines first 3 weeks by patient with clinitest tablets; then daily.

Sedimentation rate, Complete Blood Count, Complete Urinalysis at check-ups.

Repeat of any tests as indicated by clinical signs for comparison with initial base-line findings.

Blood sugar frequently in diabetic patients.

5. The special diet and supplementary medication continued.

The usual dosage pattern is shown in Table 1. Cortisone and ACTH were used according to the greater availability and other practical considerations at the time. The use of oral cortisone simplifies the problem of administration.

A preliminary period of control therapy usually was carried out in our cases. This consisted of employing either placebo injections or tablets, depending upon the route of administration to follow. With improvement, reduction of doses and substitution of placebos afforded further control of our observations. In long-term administration constant attempts were made to adjust dosage to maintain patients on the minimal amount of the compound necessary for satisfactory effects. (1-10)

CLINICAL OBSERVATIONS IN VARIOUS LOCOMOTOR DISORDERS— RHEUMATOID ARTHRITIS

Our results may be divided into two groups or periods,—early, 10-30 days; and longer-term, 30-340 days. Response was evaluated according to the therapeutic criteria of the American Rheumatism Association. (11) These results are shown in Table 2. Such evaluation is purely objective. Generally, subjective improvement was proportionate and sometimes of considerably greater degree than the objective findings, at least during the initial or early periods of administration.

In our 72 cases of rheumatoid arthritis, during the initial therapy 44% gave Grade I to II im-

provement, with 4% in complete remission. 54% showed slight improvement, and 2% no benefit.

In the follow-up intervals 55 patients had been maintained on ACTH and cortisone for one month to one year, when these figures were compiled. During this maintenance time 27% continued to be greatly improved, 17% showed no further benefit or became worse. The three patients in remission retained this response for four to seven weeks. The proportion of cases that showed slight improvement during initial hospitalization remained almost identical during the later maintenance period.

The clinical course of our patients amply confirmed the observations described by Hench and his coworkers and others.(1-10) Stiffness, pain and tenderness diminish in that order. Swelling recedes next, but usually not completely. Correlated with these effects, increased ranges of motion become evident, but coordinated movements are usually performed with greater ease even when joint mobility has not been improved to any large degree. The sense of well-being and pain-relief often are remarkable. The improvement in the performance of simple acts like standing up, getting up or down stairs, which accompanies other responses frequently may be greater than the objective evidence of benefit.

Hench has aptly termed these effects, "arthritis in miniature".(1) Even with pronounced improvement, one or more joints are likely to remain boggy, slightly swollen and somewhat tender. Frequently great symptomatic relief is observed in patients who continue to show slight or considerable articular swelling, and improvement in mobility may be noted in joints still swollen and boggy.

No other therapeutic measure has given as consistent, rapid and frequent improvement of some degree in rheumatoid arthritis as cortisone and ACTH. Unfortunately, however, symptoms return sooner or later upon withdrawal or even reduction of the adequate doses. Often the recurrent symptoms are more severe than they were originally. Even in cases on maintenance therapy, frequent booster doses may be needed to overcome "rebound" symptoms.

Our observations indicate that patients classified in Stages III and IV, i.e., the more advanced cases, are apt to show the poorest results (Tables 3 & 4), rarely a Grade I response.(11) Tables 3 & 4 present these figures in more readily visualized form. In view of the small number of cases in each column, percentages are not meant to be accurate statistical deductions. Our series contained a large number of such severe cases and our results

TABLE 1

Method of Administration of Cortisone and ACTH

1. PRELIMINARY HOSPITALIZATION

(In all cases here)

2. DOSAGE

A. PARENTERAL

1. Cortisone:—200-300 mg. I.M. for the first 24 hours (100 mg. every 8 hours); 150-200 mg. next 24 hours, then 100 mg. daily thereafter (5 mg. every 12 hours); in some cases 200 mg. daily until symptoms were adequately resolved; then the maintenance reduced gradually until sufficient for control of symptoms.
2. Adrenocorticotrophic Hormone:—100-150 mg. I.M. for the first 24 hours (25-37.5 mg. every 6 hours); 75-100 mg. next 24 hours, then 40-50 mg. daily (10-12.5 mg. every 6 hours); in some cases 80-100 mg. daily until symptoms adequately resolved; then a gradual reduction of maintenance dose level sufficient for control of symptoms.

B. ORAL

1. Cortisone:—Same doses as parenteral, increased by 25% if necessary; evenly divided 4 to 2 times a day, then 1 tablet daily or alternate days in some cases.

3. AMBULATORY FOLLOW-UP PLAN

Both continuous and interrupted methods of administration investigated.

are in conformity with the observations of Boland.(5)

Occasionally a change from one compound to another overcame symptomatic resistance or eliminated side-effects in the follow-up group. Three cases were refractory to both substances after a period of time.

RHEUMATOID-LIKE MUSCULOSKELETAL DISORDERS(1-4)

Cortisone and ACTH were administered to seven patients with severe ankylosing spondylitis (Table 5). All derived partial to complete pain relief. Stiffness was diminished in variable degrees. In all but one case chest expansion was increased. Functional capacity and range of motion were greatly improved in three cases and slightly improved in the remaining four. Three of these patients presented peripheral joint involvement, which improved markedly with the hormone therapy. In 5 cases discontinuance of the compounds was followed by a relapse within a short time.

In 4 patients with psoriasis and arthropathy the joint manifestations and skin lesions were greatly improved initially (Table 5). In each the cutaneous eruption tended to relapse on maintenance dosage and in one case it became worse. The joint involvement in two of the patients has returned to their former state while still on therapy. The other two cases have remained under satisfactory control. In this small group the articular features seemed to respond

to smaller doses of ACTH and cortisone than did the skin lesions.

In one case of non-specific ulcerative colitis with arthropathy (Table 5), the colonic and joint symptoms responded well to ACTH. Withdrawal of medication was followed by quick relapse.

The pattern of response of the joint symptoms and signs of these twelve cases of rheumatoid-like diseases was approximately similar to that of rheumatoid arthritis. The tendency toward recurrence of the active clinical picture on discontinuance of therapy was comparable to that seen in rheumatoid arthritis.

COLLAGEN DISEASES

Nine patients with "collagen diseases" were studied (Table 5). These consisted of one case of scleroderma, 3 of dermatomyositis and 2 of lupus erythematosus. In this group also are three patients with rheumatic fever now commonly included among the collagen complexes. These cases were treated with cortisone and ACTH during an initial hospital stay and some were followed for periods up to one year.

In the case of scleroderma moderate improvement in skin manifestations and articular range of motion was noted. In the three patients with dermatomyositis, improvement in their articular and other features was marked. These benefits persisted for many months after discontinuing therapy. Two cases of disseminated lupus erythematosus received the com-

TABLE 2
*Results of Administering ACTH and Cortisone In Rheumatoid Arthritis**

	Number of Cases	Complete Remission (Grade 1)	Greatly Improved (Grade 2)	Slight Improvement (Grade 3)	None or Worse (Grade 4)
Initial					
Short-term					
Hospitalization	72	3	29	39	1
10-30 days	—	—	—	—	—
		4%	40%	54%	2%
Ambulatory					
Maintenance,					
30-340 days	55	3	15	28	9
later	—	—	—	—	—
		5%	27%	51%	17%

*Evaluation of Response According to Therapeutic Criteria of the American Rheumatism Association.

pounds during an acute phase. One showed slight improvement and the other went into a complete remission lasting six months. A sudden relapse occurred while out of the hospital and, before therapy could be reinstated, the patient expired.

In all of the three cases of acute rheumatic fever with carditis there was marked subsidence of rheumatic activity during the administration of cortisone and ACTH.

GOUT

Two patients suffering attacks of acute gouty arthritis were promptly relieved by ACTH and cortisone (Table 5). One of these had been refractory to full doses of colchicine. Of four cases of chronic gouty arthritis, 2 showed only slight benefit from these compounds and one became worse. The fourth case of chronic gout derived great benefit.

In the occasional patient with an acute attack of gout unresponsive to colchicine, ACTH or cortisone may be useful. What their effects may be in chronic tophaceous gout will only be determined by long-term observations in many patients.

NON-RHEUMATOID MUSCULOSKELETAL CONDITIONS(1-4)
DEGENERATIVE ARTHRITIS OF THE HIP

Twelve cases of severe osteoarthritis of the hip were treated (Table 6). Nearly every patient had been studied by the orthopedic departments and had been referred to us as a serious

and difficult problem. All cases presented advanced changes with practically absent joint spaces in their X-ray films. Each one complained of marked limitation of motion, pain and stiffness.

Following ACTH or cortisone there was great relief of pain, definite diminution of stiffness and improved coordination of motion in nine of the twelve cases. Increased ability to perform simple acts such as arising from a chair or climbing stairs was evident in these nine patients. Only two of them, however, showed a significantly increased range of motion at the hip.

REFLEX DYSTROPHY (The Shoulder-Hand Syndrome)

Eleven cases of reflex dystrophy of the upper extremity (shoulder-hand syndrome) received ACTH or cortisone or both (Table 6). All of the patients had undergone various treatments, such as manipulation, physical therapy, stellate ganglion blocks and analgesics without satisfactory benefit.

All of the symptoms and signs in two patients were completely abolished with ACTH. In the rest of the group ACTH and cortisone afforded great improvement in five, and slight improvement in three. There was one failure.

Pain and vasomotor disturbances were rapidly improved. Limitation of motion at the shoulder responded sooner than at the hand in most cases and in patients with Stage III involvement contractures of the hands remained uninfluenced.(14)

TABLE 3

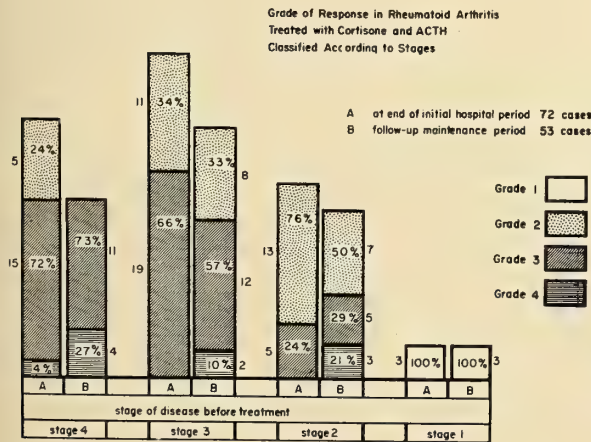
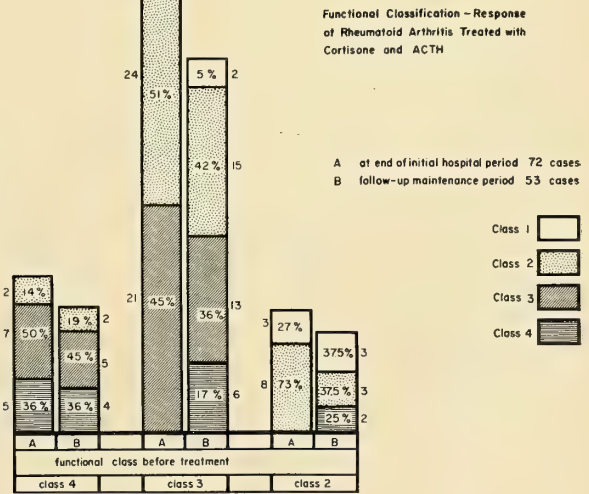


TABLE 4



In the average case of reflex dystrophy larger early doses of cortisone and ACTH were needed than in the other conditions reported here. These patients required maintenance therapy for 1-5 months before it could be discontinued entirely. Seven cases have been followed for periods up to eight months since cessation of therapy without a relapse.

PERIARTHRITIS OF THE SHOULDER ("Frozen Shoulder")

Fourteen patients with periartthritis of the shoulder (periarticular fibrositis) were given cortisone and ACTH with or without manipulation under anesthesia (Table 6). Eleven were started on these drugs. Three first received them after manipulation. Six of the eleven cases started on the compounds recovered completely. Of the five failures, three were subsequently manipulated, with complete recovery in one.

Of the three other patients who received cortisone after manipulation, two recovered completely; the other was unresponsive.

Nine of the fourteen cases, therefore, showed a complete response after the use of ACTH or

cortisone in one way or another, and it has persisted after discontinuation of therapy. All of the patients receiving these compounds experienced effective pain-relief. However, in evaluating our results, only greatly increased active range of motion was considered a good effect.

All of these patients were severe, refractory cases with great pain and limitation of motion who had failed to respond to the conventional forms of treatment.

CALCIFIC TENDINITIS AND BURSITIS OF THE SHOULDER (Table 6)

One case with typical acute calcific tendinitis of the supraspinatus tendon was given cortisone. Pain was relieved in the first day and shoulder disability was greatly improved within 72 hours.

In a case of chronic calcific tendinitis with periartthritis, great decrease of pain and tenderness was noted within one week. Two months of maintenance therapy sustained the effects. No change in the calcific deposit was noted in either patient.

These 2 cases are suggestive, but do not represent a significant experience.

TABLE 5
Results In Rheumatoid-Like Diseases

	No. Cases	ACTC	Cort.	Over-All Results*			
				Great	Slight	None	Worse
ANKYLOSING SPONDYLITIS	7	1	6 (1 both)	3	3		
PSORIATIC ARTHROPATHY	4	2	2 (1 both)	4			
GOUTY							
ACUTE	2	1	1	2			
CHRONIC	4	2	2 (1 both)	1	2		
ULCERATIVE COLITIS WITH ARTHRITIS	1	1		1			
COLLAGEN DISEASES	9	5	4	7	2		
(all short-term observations)							

*No complete remissions, except in Ac. Gout.

TRIGGER FINGER (Table 6)

In two cases of rheumatoid arthritis with co-incident constrictive tendovaginitis ("trigger finger") of long-standing duration, no benefit was noticed from cortisone or ACTH on the "trigger-finger". It is possible that in earlier involvement of this nature more satisfactory effects may be obtained.

ORTHOPEDIC PROCEDURES WITH ACTH AND CORTISONE(12)
SURGICAL

We have observed six cases who have undergone surgical procedures while they were on cortisone or ACTH therapy. The work of Ragan(7) and coworkers on delayed wound healing with these substances poses the problem as to whether interruption of therapy is necessary in patients undergoing surgery.

In our series of two arthrotomies, two biopsies and one incision and drainage of an abscess, healing occurred normally without interruption of steroid administration. In a case of bilateral bunion operation with the additional removal of

a subcutaneous nodule at each hand, therapy was discontinued five days post-operatively owing to oozing of two of the wounds.

CONTRACTURES AND POST-MANIPULATION
USE OF ACTH AND CORTISONE

The influence of cortisone and ACTH on the correction of contractures is under study at present, but sufficient time has not elapsed for an evaluation of results. The relief of pain, inflammation and muscle spasm enables active and passive physiotherapy and manipulation to be carried out in patients who previously could not tolerate such procedures. It would appear that ACTH and cortisone may be valuable adjuncts to other therapeutic measures in the management of contractures. Their influence on existing or developing fibroplasia may insure better results with exercises, manipulation and other orthopedic procedures, especially musculoskeletal surgery, as we already have discussed with regard to periarthrits of the shoulder.

TABLE 6
Results In Non-Rheumatoid Conditions

	No. Cases	ACTH	Cort.	Complete	Over-All Results		
					Great	Slight	None
DEGENERATIVE ARTHRITIS (HIP)	12	2	10		1	8	3
SHOULDER-HAND SYNDROME (REFLEX DYSTROPHY)	11	5 (1 both)	6	2	5	2	2
PERIARTHRITIS OF SHOULDER*	14	6 (1 both)	8		8	1	5
CALCIFIC TENDINITIS AND BURSITIS OF SH.	Acute 1 Chron. 1		1	1			
			1		1		
TRIGGER FINGER	2	1	1				2

*Manipulation under anesthesia in 5 cases.

PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL HOSPITAL CASE NO. 28342

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the New England Journal of Medicine. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A seventy-year-old man was admitted to the hospital because of persistent hematuria.

Three months before admission, the patient slipped while walking and twisted his right side. Following this, he had slight pain and an ache in the right flank that disappeared after several days. At that time, he noticed the onset of hematuria, persistent to the day of admission except for a single period of three weeks. The degree of hematuria varied considerably and occurred during all parts of micturition. There was no dribbling, hesitancy or incontinence. A slight burning occasionally accompanied urination, and the patient occasionally suffered with nocturia and frequency.

Two months prior to admission, he was cystoscoped in the Out Patient Department and found to have a papillary growth of the bladder 1.5 cm. above the left orifice.

For three weeks before admission, the patient had an uncomfortable feeling in the left groin, and three days prior to entry he suffered with low midback pain lasting a day.

The past and family histories were irrelevant.

Physical examination revealed a well-preserved elderly man in no distress. Examination of the lungs and heart was negative except for a systolic murmur at the apex and over the aortic area. The abdomen was soft, and no masses were felt.

The blood pressure was 150 systolic, 92 diastolic. The temperature, pulse and respirations were normal.

The urine showed a 4 plus test for albumin, a few white blood cells and many red blood cells. There were no casts, and the concentration was good. A culture of the urine revealed a few colonies of *Staphylococcus albus*. Examination of the blood showed a red-cell count of 4,250,000 with 75 per cent hemoglobin, and a

white-cell count of 6300 with a normal differential. The nonprotein nitrogen was 23 mg. per 100 cc., and the prothrombin was normal. The phenolsulfonephthalein test showed 35 per cent excretion in fifteen minutes, and an additional 15 per cent in half an hour. X-ray films of the skull and chest revealed no lesions resembling metastases.

Cystoscopy failed to reveal the papillary growth of the bladder previously seen in the Out Patient Department. An intravenous pyelogram showed delayed excretion of the dye, which faintly outlined the ureters and kidneys. The bladder outline was relatively smooth; there was a slight defect at the base consistent with an enlarged prostate. A retrograde pyelogram demonstrated bilateral pressure defects along the upper surfaces of both kidneys. However, the lower poles were relatively normal.

Operation was performed on the fourth day after admission.

DR. GEO. A. WILLIAMSON

This case would seem to be a fortunate one to have to discuss because there is only one symptom to be analyzed. Haematuria, which has persisted for three months in a seventy year old male, would limit the pathology to the genitourinary tract and the patient's age limits the variety of pathology to that which would occur in the older age group.

There was an injury at the time of the onset of symptoms, but it does not seem to have been of any great severity. It is described as a slip causing him to twist his lower back and no mention is made of any symptoms of acute pain, muscle spasm or functional limitations in his activities. The slight pain in his right flank disappeared after a few days leaving only the haematuria with occasional nocturia and frequency. We note from the history as contained in the protocol that blood was present in the urine in all phases of micturition indicating that the source of bleeding was probably in the upper urinary tracts.

One month after the onset of haematuria, a papillary growth 1.5 centimeters above the left ureteral orifice was found at the time of an outpatient cystoscopic examination. We are not told whether the growth was removed for examination by the pathologist or was destroyed by fulguration at the time of this bladder inspection. At any rate, apparently his bleeding continued and about one month and a half later he devel-

oped some discomfort in the left groin and mid-lumbar region lasting for only one day. It was apparently not severe enough to make any great impression and, therefore, could not have been a renal colic.

He was admitted to the hospital because of his persistent haematuria along with some mild discomfort in the midlumbar region and left groin.

His physical examination at the time of admission did not show any remarkable weight loss or distress such as might be expected from most malignant processes or serious infectious conditions. As far as the chest, heart, and abdomen were concerned, no evidence of pathological changes or unusual complaints are mentioned. Blood-pressure, temperature and respiration were entirely normal.

The urine showed three plus albumen, a few white blood cells, many red blood cells, no casts and the concentration was good. The P.S.P. test of 50% in the first half hour is a normal result.

The blood chemistry and blood counts were normal indicating the lack of any deficiencies in kidney function.

X-rays of the chest and skull were negative for any evidence of metastatic new growths.

A cystoscopic examination was made after admission and showed what might be considered as a normal bladder for a man of his age and no signs of the papillary growths previously mentioned were noted.

Retrograde pyelogram showed pressure defects along the upper surfaces of both kidneys with the lower poles relatively normal. There was no residual urine in the bladder and no definite source of bleeding from the bladder or either ureter could be discovered. The only definite finding was the pressure defects along the upper surfaces of both kidneys with the most marked pressure along the superior calix on the left side.

A consideration of the causes of haematuria may lead us to the diagnosis:

I. *Haematuria from urinary tract.*

- (1) *Renal causes:* (a) If the bleeding is scant we can look for calculi, tuberculous, hydronephrosis, polycystic kidney, acute pyelitis, or nephritis, injury or the effects of drugs on the kidney tissue such as sulfanilamides, urotropine, etc.

(b) If the bleeding is profuse, we must consider

1. Malignant tumors of the kidney
Hypernephroma
Carcinoma of kidney or pelvis
Sarcoma
2. Innocent tumors—papilloma or angioma of pelvis
3. Calculus and tuberculosis may also be considered
4. Injuries to the kidney
5. Essential haematuria
- (2) Ureteral causes: calculus or neoplasm of the ureter
- (3) Bladder causes: malignant or benign papilloma or carcinoma of prostate, tuberculosis of bladder or prostate, calculus, acute cystitis, injury or parasites.
- (4) Urethral: acute urethritis or impacted urethral calculus, papilloma, naevus, or caruncle of urethra.

II. *Haematuria from disease of neighboring organ.*

1. Carcinoma of uterus, vagina, rectum.
2. Acute salpingitis or appendicitis.
3. Pelvic abscess.
4. Tuberculosis of intestine or diverticulitis of intestine.

III. *Haematuria in general diseases.*

1. Renal infarction in endocarditis.
2. Arteriosclerosis.
3. Leukaemia.
4. Purpura.
5. Scurvy.
6. Haemophilia
7. Acute fevers such as malaria, etc.

We may usually expect some additional symptoms in haematuria which will assist in locating the cause of the bleeding.

The information given to us indicating that the bleeding was apparent in all stages of micturition would indicate that the course of bleeding was probably located in the kidney region rather than from the lower urinary tract.

On cystoscopic examination, no lesion was found in the bladder from which the haematuria could have emanated. Although we are not told that blood was seen to come from either ureter at the time of examination, we must assume that it was of renal or ureteral origin. The functional tests were normal and the N.P.N. showed no elevation. The patient's age and

lack of sufficient urinary symptoms leads me to discard tuberculosis of the kidney, renal calculi, acute nephritis or pyelitis as a cause of the bleeding. The injury he is reported to have had was not severe enough to produce direct damage to the kidney parenchyma sufficient to produce all this haematuria. Polycystic kidney and damage to the kidney parenchyma by medications such as urotropin, or sulfanilamids, etc. are also discarded because of lack of symptomatology or history.

Pathology of or in the ureters, bladder or urethra may be passed over because of the type of the bleeding, the lack of acute inflammatory or colicky symptoms, and the negative results in these areas of the cystoscopic examination.

As genito-urinary causes of the haematuria, we are left with the possibility of neoplasms of the kidney.

There are extra-renal factors involving neighboring organs as we have seen from the table of causes of haematuria. None of these need be considered at this time because of the lack of symptoms relating to the intestinal tract where related pathology might be found.

The possibility of some general disease must be reviewed. The blood diseases and acute fevers may be ignored in the face of our normal laboratory findings and the absence of additional symptoms of any other diseases.

Returning to the kidney and to tumors of the kidney, we have the problem of haematuria of at least three months duration, which, however, has had little, if any, effect on the general health of the patient or upon his renal functions. The lesion is so placed that it involves the region of the upper poles of both kidneys and is, therefore, a bilateral renal tumor, bilateral suprarenal tumor, retroperitoneal tumor producing extra renal pressure, or haemorrhage from trauma to the kidney producing a partial rupture of the parenchyma.

Tumors of the kidneys may be classified as:

- (1) Cysts.
- (2) Benign tumors such as fibroma, lipomas, angiomas and adenomas.
- (3) Malignant tumors which occur in
 - (a) Childhood (birth to 5 years).
Embryonal or (Wilms tumor).
 - (b) After 40 years: Hypernephroma
Adenocarcinoma
Sarcoma
- (4) Malignant tumors in the pelvis and ureter.
 - Papilloma of renal pelvis—benign with malignant possibilities.
 - Papillary carcinoma
 - Squamous cell carcinoma

The benign tumors are uncommon and usually do not produce symptoms until they attain considerable size but most of them are found, incidentally, at postmortem. The Wilms tumor, which is a mixed embryonal tumor, is found almost entirely in children although a rare case has been reported in the adult.

Of the malignant tumors, the hypernephroma is the most common. Its onset is insidious with haematuria as the earliest and in many cases, the only symptom for some time. Metastases are common and the symptoms produced by the secondary foci are frequently what brings the patient to the doctor for care. The outlook is poor and the only treatment is nephrectomy in the early cases.

The report of finding a papilloma in the bladder at the time of the original cystoscopic suggests the possibility of an implantation in the bladder of a pelvic or ureteral tumor. I assume that the urologist destroyed it at the time as it was not seen on subsequent examination.

I cannot substantiate a diagnosis of trauma to the kidney or pressure on the kidney by retroperitoneal growths.

My diagnosis: Primary tumor of the kidney, malignant, probably hypernephroma.

DIFFERENTIAL DIAGNOSIS

Dr. George G. Smith: The question in this case is whether a twist of the torso sustained while the patient was walking, without any actual fall, could cause bleeding from trauma of a normal kidney. I do not believe it would. I think it might if the patient had renal stone or hydronephrosis or some pathologic condition in the kidney, which might be ripped or torn by any unusual motion.

The fact that the bleeding occurred during all parts of micturition is rather against a prostatic origin. Usually, blood from the prostate precedes urination—not always, but usually, furthermore, there was no dribbling, hesitancy or incontinence, and nothing to substantiate a diagnosis of prostatic bleeding.

The answers to two questions would be helpful. Did the patient have any bladder residuum? Was the blood seen coming from the ureter or any particular source at the time of cystoscopy?

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RESEARCH IN THE
SERVICE OF MEDICINE

Dr. Tracy B. Mallory: Can you answer either of those two questions, Dr. Gens?

Dr. John P. Gens: There was no bladder residuum, and no blood could be seen coming from either ureter at the time of cystoscopy.

Dr. Smith: Was the patient bleeding at the time?

Dr. Gens: No.

Dr. Smith: It is a good thing to cystoscope patients with hematuria at the time there is blood in the urine, because then one can get an indication of the origin of the blood, which one often cannot get later on.

The fact that cystoscopy failed to reveal the papillary growth probably means that the alleged papilloma was a blood clot adherent to the bladder wall. It is very difficult to distinguish between an adherent blood clot and a papilloma that has been bleeding and is infiltrated with blood. With kidneys that show as good a renal function by nonprotein nitrogen and phenol-sulfonephthalein tests as this man's kidneys did, one expects to see a very good picture of the kidney pelvis from the Diodrast or Neoskiodan, whichever one was used, unless he was not well prepared and had a great deal of fluid.

From the story to date I have not the slightest idea what this man was operated on for. May we see the x-ray films?

Dr. Laurence L. Robbins: These are the films of the intravenous pyelograms, and as noted, there is no good visualization of the calyces, pelves or ureters. The retrograde pyelogram, in contrast, shows these very obvious bilateral pressure defects in the outlines of both pelves. They are nearly symmetrical, but there is more involvement of the superior calyx on the left.

Dr. Smith: They are excellent and unusual films, I should say. The simultaneous bilateral occurrence of tumor is possible, but very unusual. It is much more likely that the patient had bilateral solitary cysts. The pelves and calyces do not give the picture of congenital polycystic kidneys. Furthermore, the renal-function tests are too good for a case of polycystic kidneys in a man of this age. On the other hand, there is very definite pressure here, as Dr. Robbins has pointed out. The uppermost calyx is thinned out over a presumably smooth,

symmetrical round tumor. It is quite possible to get marked hematuria from solitary cyst of the kidney, perhaps owing to interference with the blood supply, sometimes with rupture of the cyst. I should make a diagnosis of bilateral solitary cysts of the kidneys. I do not know which side I should operate on or why, but that is my diagnosis.

Dr. Mallory: Would you have operated on this patient on this evidence?

Dr. Smith: I suppose he could have had a tumor on one side and a cyst on the other, but it would be unusual to have the findings so symmetrical. If he had had successive episodes of bleeding and if observation had shown that he always bled from one side, I should be inclined to operate on the side. If it were a tumor, I should take out that kidney, and if it were, as seems more probable, a solitary cyst, I believe that removal of such a cyst would check the hemorrhage and that it would do to the patient's advantage to operate.

Dr. William B. Breed: Without that evidence, where would you operate?

Dr. Smith: As I say, I should want to know from which side the bleeding was coming. We do not know that from the history.

Dr. Breed: Well, where are you going to operate—midline, right or left?

Dr. Smith: I should guess that the left kidney would be the one to pick because the upper calyx appears to be more involved in the x-ray film than the one on the other side, but I do not believe that is sufficient reason for selecting that side. I should insist on knowing which side was bleeding and if this elderly man stopped bleeding and had no symptoms, I should leave him alone.

Dr. J. Dellinger Barney: What about bilateral adrenal tumors?

Dr. Smith: These lesions very evidently involved the structure of the kidney itself—the parenchyma of the kidney. So far as I know, adrenal tumors do not do that; they push the kidneys down but do not invade them.

Dr. Fletcher H. Colby: It would add to the interest of the discussion if Dr. Smith were told the next step.

Dr. Mallory: We are prepared to do that. Dr. Gens, will you proceed?

Dr. Gens: We never did know from which

side the bleeding was coming. When the patient was admitted to the hospital, the gross hematuria stopped. The urine on both sides showed red blood cells. We decided to operate on the right side because we believed that the chance of cyst was greater on the left side since the calyces were actually involved on the left side, whereas the tumor was pushing the pelvis or the calyx away on the right side, which would be more like neoplasm. Therefore, we operated on the right side, came down on a cyst and treated it in the usual fashion.

Dr. Mallory: Would you then wish to do anything more Dr. Smith?

Dr. Smith: I should assume that there was a cyst on the other side also, and unless he bled again or had further symptoms, I do not believe I should operate.

CLINICAL DIAGNOSIS

Cortical cysts of kidneys.

DR. SMITH'S DIAGNOSIS

Bilateral solitary cysts of kidneys.

ANATOMICAL DIAGNOSIS

Solitary cyst of right kidney.

Papillary adenocarcinoma of left kidney.

PATHOLOGICAL DISCUSSION

Dr. Mallory: Suppose you go ahead with the story, Dr. Gens.

Dr. Gens: About seven days later, although the patient had a perfectly uneventful immediate postoperative course, he once more had gross blood in the urine.

Dr. Smith: May I ask what you did to the right kidney?

Dr. Gens: We excised the wall of the cyst. Then we decided to aspirate the left side but did not obtain anything but a few drops of blood, although we were fairly certain that we had touched the tumor mass in the left kidney.

Dr. Smith: But you knew the blood was coming from the left side?

Dr. Gens: No.

Dr. Smith: I believe I should have looked in the bladder to see if the blood were coming from the left side.

Dr. Mallory: I think by exclusion it was believed that the hemorrhage must have been coming from the other side.

Dr. Smith: I think that is assuming too much; however, it probably was so. But I do not believe one can take anything that is easily demonstrated for granted. One could easily put in a small cystoscope and look at the ureters.

Dr. Mallory: Eventually, the patient was explored on the left side, an obvious tumor was found, and a nephrectomy performed. He made an uneventful convalescence. The tumor proved to be a papillary adenocarcinoma of renal origin.

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

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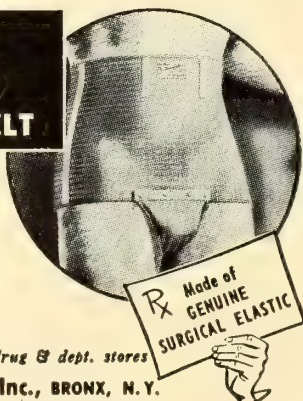
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Editorial

POST MORTEMES

The status of the practice of medicine in a hospital, a community, or even during an era of time coincides fairly closely with the percentage of autopsies which are performed in those situations. It may be that the status considerably depends upon the percentage.

Autopsies are usually not requested by the relatives. They are too often not urged by physicians. They are quite often not considered necessary by the coroner or medical examiner.

Autopsies are obtained most often by a man with a fine medical curiosity, and the drive necessary to overcome the inertia or obstruction which kinfolk feel after a death. A hospital with 60 to 70 per cent autopsies is bound to be a good teaching institution with an alert staff. It probably also has at least one 'ramrod' to urge or heckle the less eager members in non-medico-legal cases.

There must be legal authorization for an autopsy. The limits and exact rules are often vague in the minds of physicians, both long-time and recently in practice. The rules are actually quite clear and simple, both as they apply to deaths from natural causes or from violence or casualty.

The best brief summary of the 'Legal Authorization for Autopsy' which has appeared in recent times is that of Louis J. Regan, M.D., L.L.B., of Los Angeles. The report was read at the American Academy of Forensic Sciences in Chicago, March 1st, 1951, and published in the *Annals of Western Medicine and Surgery* for April, 1951. It contains the provisions for autopsy in each of the states, and an epitome of the rules. *The provisions as they affect Arizona are listed as follows,—*

ARIZONA

I. AUTHORIZATION

A. Coroner. 1949 Laws, Ch. 39, Sec. 1

Any person shall report death without medical attention to a peace officer who shall investigate and report to the coroner, who may and, upon request of County Attorney, shall direct the medical examiner or any other qualified physician to make such examination of the body as may seem necessary to determine the cause of death. The medical examiner or physician shall report the findings to the coroner and County Attorney.

The coroner may sign the death certificate, stating the cause of death, or may direct the medical examiner to do so.

Where there is a suspicious death, inquest is to be held with six to twelve jurors. (R.C. 1928, Sec. 5272).

B. The Superintendent of the State Prison may, with the consent of the governor, dispose of bodies or portions thereof, of persons executed at the State Prison and not claimed by relatives or friends within 24 hours, for scientific purposes to any recognized institution for scientific research. (Rev. R.C. 1928, Sec. 5132).

C. Workmen's Compensation Act. No statute.

D. Private Individual. No statute.

E. Insurance. No statute.

New York Life v. McNeeley (Ariz.), 72 Pac. (2d) 948. An insurance case. The issue, to decide whether death was by accident or suicide. The wife of the deceased requested an autopsy and it was performed by the coroner under Sec. 68-606, and used as evidence.

II. PERFORMANCE

A. *By any qualified physician.*

B. *By the medical examiner.*

The Board of Supervisors may, upon request of the County Attorney, or the coroner, appoint a medical examiner to examine the body of any person believed by the coroner to have died through criminal means. The person appointed must be a qualified and practicing physician and surgeon.

III. LIABILITY

A. Criminal.

Sec. 43-5201: Provides that every person who mutilates a body without authority of law or removes a body with intent to dissect it without authority, is guilty of a felony. (R.C. 1928, Sec. 4652).

B. Civil. No statute.

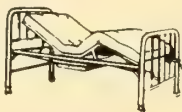
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The phrase 'by any qualified physician' gives a wide leeway in case of need. It is certain, however, that most of the examinations should be, and are, made by physicians trained in pathology and with the equipment to examine the tissues. Arizona hospitals are constantly becoming better able to complete the requirements for post mortem studies.

In addition to the laws mentioned by Dr. Regan, there is now a law (reported elsewhere



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in this Journal) which provides for an Anatomy Board and for the regulation of cadavers for dissection. This law, originally House Bill No. 83, contains one reference to post mortems. It states that there shall be certain exceptions to the rules which require reporting and delivery of corpses,—"Nothing in this Act shall be construed to prevent any hospital, duly incorporated college or university or any duly licensed physician, surgeon or dentist from acquiring by gift or otherwise from persons having lawful authority to dispose of the same the dead

body of any human being *for the purpose of post mortem examinations*, dissection or other scientific use."

The availability of a cadaver for dissection is equally as valuable as an autopsy in the education of a medical student. It is wise for Arizona to have the enabling laws in case a medical school should become possible. Meanwhile the answer to many medical problems, and one of the greatest aids to post-graduate medical education, is the autopsy—but you have to take the trouble to get permission for it.

TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER, M.D.

The newest sensation in the commercial vitamin ranks ('Hadacol') has the same old appeal as the tonics in great-grandfather's day. . . . It was worth a chuckle in 1930 to find a dozen bushel-baskets of old tonic bottles in the attic of an ancient bow-roofed house on Cape Cod. All of the bottles had well-known patent medicine names, and all had one common ingredient—a 10 to 20 per cent content of alcohol. . . . Now a liquor commissioner near Chicago has ruled that licensed liquor stores, not drug stores, must handle Hadacol, since it contains 12 per cent of the stuff.

After a recent paragraph about the late DR. FENNER of Tucson, a few more pieces of data were sent in by a Sister from St. Mary's Hospital. . . . Dr. Fenner joined the Staff there in 1885—a long time ago in this area. Actually, about fifteen years after Custer's massacre, and during the presidential years of Cleveland . . . Dr. Fenner drew the plans for the older portions of St. Mary's including the circular Sanatorium building, erected in 1900. Dr. Meade Clyne worked with him, and Dr. C. A. Thomas is said to have taken over the Southern Pacific work from him in 1919. . . . The later development of the S.P. facilities would be a story in itself. Dr. Thomas should write it.

No one should be surprised when medical terminology is obscure. Now and then, however, a term pops up which is unfamiliar, but some one knows it well enough to write an article about it. . . . Dr. George Park of Chicago tells of "A Case of Simulated Dyslexia" in a pediatrics journal. Not just 'Dyslexia', but **SIMULATED** dyslexia! . . . The case was that of Junior, in a

mental and emotional snarl because of parental demands. So, he developed **READING DIFFICULTY**. . . . Another small item of amazement,—the Wesley Memorial Hospital in Chicago has a **Dyslexia Memorial Institute**.

A medical trade journal states that '**NUISANCE FEES**' are a poor idea. Charging for a telephone call in order to discourage patients who are overly nervous, or 'free-loaders,' can cause ill-will which overbalances the value. . . . The Rocky Mountain Medical Journal believes that the physician who uses them takes a notable chance.

The Commercial Solvents 'Reporter' tells of the value of **ORAL PENICILLIN THERAPY**. It is said to be effective, convenient, and economical. . . . Twenty to 30 per cent of the ingested drug is absorbed into the blood stream. Keefer is quoted on the dosages effective in several infections,—Gonorrhea—100,000 U. twice a day. Erysipelas—200,000 U. three times a day. Scarlet fever, tonsillitis, otitis media—200,000 U. three times a day. Staphylococcal infections—400,000 U. three times a day. Pneumococcal infections—200,000 to 400,000 U. three times a day. Vincent's Angina—200,000 U. three times a day.

THE AMERICAN ASS'N. FOR THORACIC SURGERY produced several points of interests this spring. . . . Segmental resection of the lung has reached the point where a Saranac group removed six wedges from one patient. . . . 'Mucoid impaction' of the bronchi is a newly named clinical entity, reported from Dallas. . . . Resection of an upper lobe with a thoracoplasty at the same opera-

tion has numerous advantages, says an Oregon surgeon (confirming Samson of San Francisco). . . . Pulmonary function changes are not predictable after pneumonectomy, show increasing limitation after thoracoplasties, are surprisingly severe after intrapleural pneumothorax, but are scanty and stable after extra-pleural pneumo and oleothorax.

The promise which ACTH provides for those miserable patients with chronic dermatitis (and for their depressed physicians) looms up as a grand relief. Remember those scaling, swathed and faceless wretches with exfoliative dermatitis in the large hospital wards? With pemphigus? With psoriasis? Or even those people with recurrent contact dermatitis? . . . They say the effect is thru protection of collagen in the skin; in blocking of hypersensitiveness; in suppressing inflammatory reactions.

So you took up medicine because you liked it, or to make a living? Think again; it's not so simple. . . . Dr. Bernard Strauss reports in the New York State Journal of Medicine that the individual's reasons are as follows.—1. Prestige-hunger. 2. The need to be authoritative. 3. The need to be omniscient. 4. The need to 'Do Good'. 5. The need to be loved. 6. The need to rule, dominate, subjugate. . . . Only one or two of these seem kindly and respectable reasons—but maybe Dr. Strauss was motivated by Numbers 2 and 3.

Note from the Michigan State Medical Journal, Livestock bitten by RABID CARNIVORES are unlikely to develop the disease and may be safely slaughtered within one week, or after six months. The only risk is to the handlers of the live animal or carcass, not to the consumer.

ARIZONA MEDICINE articles are used in other publications with increasing frequency. . . . Abbott's beautiful 'What's New' makes a spread out of the use of diethylstilbestrol for threatened abortion, recently reported in our journal by Karnaky.

The Pfizer Company reports that aureomycin may or may not be of value in proved cases of HERPES SIMPLEX. Too few cases, so far. . . . Aureomycin and chloramphenicol and a placebo had the same lack of effect on HERPES ZOSTER, tho it modified and shortened the pustular stage.

Ebert of Minneapolis, on emphysema.—Patients with SEVERE EMPHYSEMA may become dependent on oxygen. This is in part due to the relief obtained, but also is in large part psychological. There is no evidence of true addition.

About a year ago it was mentioned here that experimental work was being done at St. Luke's Hospital, Chicago, on ACTH in DISEASES OF THE LIVER. . . . Several months ago Webster of New York demonstrated a permanent regeneration of the injured liver in several types of disease after use of ADRENAL CORTEX EXTRACT. . . . Side effects were common, but the repair and the improvement in CH-protein metabolism make further study worth while in cirrhosis and hepatitis. . . . It may be wise to use purer materials, but the results from the extract allowed the drug to be stopped, in this small series, in contrast to the use of cortisone and ACTH.

Austrian and seven colleagues from Baltimore experimented with DOSAGES OF PENICILLIN IN LOBAR PNEUMONIA. . . . They have found that cases which were given 300,000 units of sodium G penicillin intramuscularly on the first dose (plus Benemid to delay excretion) and then 300,000 U. plus Benemid by mouth every 12 hours, did just as well as when all of the penicillin was given I.M. . . . This should interest Dr. Cambier of Tucson who helped Dr. Tillett, on the first work of its kind, several years ago in New York.

Lynch and Karon have told of a successful TREATMENT OF WARTS, especially plantar warts or those around nails. . . . They use an ointment composed of formalin in aquaphor. The lesions are treated twice a day by the patient, shaved twice a month by the physician. . . . Anyone having professional contact with formaldehyde is excluded from treatment to avoid the hazards of sensitization.

A side effect of AUREOMYCIN AND TERRAMYCIN results from the very broadness of their spectrum—and from the limitation of even the broadest. . . . When you aim a drug at a virus or coccus in the bronchi, you KNOCK OUT THE COLIFORM BACTERIA IN THE INTESTINAL TRACT. . . . As previously mentioned here, a monilia infection may occur in its wake, but more commonly one may simply have gas, cramps, and diarrhea.

Dr. Most and his colleagues have reported that Terramycin is 100 per cent effective against AMEBIASIS. They suggest simultaneous mass treatment in hospitals and institutions where the incidence is high.

Resistance of staphylococcal strains to penicillin occurs more often in superficial than deep-seated infections, more often in hospital in-patients than outpatients, and as often as 38.5 per cent of the nasal cavities of hospital physicians and 75 per cent of the nurses in a German hospital.

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REPORT OF THE DELEGATE

House of Delegates, American Medical Ass'n.
Atlantic City, N. J., June 11-15, 1951.

The annual session of the A.M.A. in Atlantic City had a registration of 28,398 persons—12,229 physicians and 16,167 guests and others. This compared with a total registration of 23,777, including 10,241 physicians in San Francisco last year.

The House of Delegates met on June 11, 13 and 14. Several important announcements were made to the House by the Chairman of the Board of Trustees and by the President, Dr. Henderson, during the opening sessions.

Dr. Louis H. Bauer, Chairman of the Board of Trustees, was elected to the office of President-Elect. During the meeting of the House of June 11, he announced that the Board of Trustees "being duly cognizant of the necessity of seeking and, if possible, anticipating the needs of the public, has decided to appoint an advisory committee of *laymen* to give advise to the Board of Trustees on problems in the field of medical care and to present the viewpoint of the general public. The Board intends to appoint individuals, representatives of lay fields, such as industry, labor, agriculture, education, the legal profession, and the clergy—who who are not engaged in politics and are so outstanding that their opinions will automatically receive respect."

In his report to the House, Dr. Henderson announced that the Campaign Coordinating Committee, and the Board of Trustees had decided to terminate the National Educational Campaign at the end of this year. But the House of Delegates apparently believed such a move too dangerous at this time because, immediately, several resolutions were introduced urging the Board to retain Whitaker and Baxter for another year. The Board of Trustees acted favorably, and on the final day of the House meeting, announcement was made that the public relations firm would serve thru 1952 on a part time basis. The Campaign Coordinating Committee was retained also, and will be headed again the following year by Dr. Henderson.

Dr. John W. Cline, San Francisco, was inducted into the office of President of the A.M.A. for the ensuing year. His inaugural address was broadcast to the nation over two national networks. His address dealt almost exclusively

with the A.M.A., its aims and objectives. To have heard him, one could not have helped but feel proud that he was part of such a truly American institution, democratic in organization, and dedicated to high purposes.

Dr. Dwight H. Murray, of Napa, Calif., will succeed Dr. Bauer as Chairman of the Board of Trustees. He has been on the Board for some years, and Chairman of several important committees of the Board, including the Legislative Committee. Dr. David B. Allman, Atlantic City, was elected to the Board to fill the unexpired term of Dr. Bauer, and Dr. Walter B. Martin, Norford, Va. was re-elected to the Board for another five years.

The House of Delegates acted upon many resolutions, and a complete summary of its actions have appeared in the June 30 and July 7 issues of the A.M.A. Journal.

A review of the action of the House on some of the more important resolutions will be briefed in this report:—

1. Adopted a resolution which supports federal financial aid to medical schools for construction only, based on the formula of the Hill-Burton Hospital Construction Act.

2. Authorization to expand the A.M.A.'s Physician Placement Service thru which many communities may obtain assistance in obtaining the services of a physician.

3. Adoption of a resolution which urged a "thorough investigation" of activities aimed at indoctrination of students in grammar school, high school and college with the insidious and destructive tenets of the welfare state."

4. Approved a report from the Board of Trustees which stated that a Joint Committee of the American Medical Association, the American College of Physicians, the American College of Surgeons, and the American Hospital Association had been appointed, to draft a basic plan for the cooperative program in the field of hospital standardization. This group is called the Joint Commission on Accreditation of Hospitals. Basically, this Commission will have three representatives of the A. C. of P., three from the A. C. of S., six from the A.M.A. and six from the Amer Hospital Assoc; with the way left open for the Canadian Medical and Hospital Associations to have representatives on the Commission, since both Colleges and the American Hospital Assoc. number Canadian members in their organizations.

The Joint Commission on Accreditation of Hospitals will formulate standards, determine the type and scope of inspections, allocate hospitals for inspection to the several participating organizations, maintain records and award all certificates of accreditation. Inspections will ordinarily be made by the field staffs of constituent organizations and may be combined with other inspections made by these organizations for other purposes, such as approval for intern and resident training.

The Regents of the A. C. of P., and the A. C. of S., have approved the proposal for the establishment and financing of the Joint Commission on Accreditation of Hospitals. Similar consideration of the proposal will be given by the American Hospital Association at its annual meeting in September, 1951.

The Reference Committee on Medical Education and Hospitals in its report to the House discussed the various problems relating to hospital standardization, and made several suggestions to the Board of Trustees in its further study of this problem, so that the best interests of all divisions of the medical profession will be amply protected. The reference committee was especially anxious that general practitioners be represented on the voting body of the A.M.A., and that an advisory committee be formed consisting of representatives from all the scientific sections of the A.M.A. This committee called attention to the desirability of having inspections, discussions and accreditation from the point of view of the medical professional aspects of hospital care be carried out only by the medical representatives on the Commission, and that the Board of Trustees convey this philosophy to those representatives after the Commission has actually been formed. As a step to implement this suggestion, the reference committee recommended that the voting power of the Commission be re-arranged as follows: three representatives from the A. C. of S., three from the A. C. of P., four from the A.H.A., and eight from the A.M.A.

5. The House approved announcement of the Board of Trustees relative to the expansion of the A.M.A. Public Relations Department. Mr. Leo Brown, formerly Public Relations Director for the Medical Society of Pennsylvania, has assumed the office of Executive Director. Also, an advisory committee to the Director of the Public Relations Department, composed of exe-

cutive secretaries or public relations directors of eight constituent state medical associations, has been appointed. Ohio, Indiana, Michigan, Colorado, California, Oklahoma, Wisconsin, and New York have representation on this Advisory Committee.

6. The House adopted the report of the Reference Committee on Amendments to the Constitution and By-Laws relative to establishment of Single Membership Classification in the A.M.A. Several resolutions were introduced relative to this matter, which provided for equal rights and privileges by all active members, and eliminating "Fellowships" upon application, acceptance and payment of \$5.00 extra dues in addition to the \$25.00 each active member pays for membership in the A.M.A. The reference committee approved in principle the content of these resolutions, especially as to eligibility of membership to take part in organizational and scientific programs of the A.M.A. without the necessity of other than regular membership, and this report was adopted. However, the Committee felt that there is a definite question of the advisability of abandoning the term "Fellowship," and recommended that this matter be referred to the standing committee of the House on Constitution and By-Laws, with instructions to prepare such changes in the By-Laws, in consultation with the Board of Trustees, as may be necessary to carry out these recommendations.

7. Approval was given to resolutions dealing with Emergency Medical Service, such as established by many county medical societies for the purpose of rendering better community medical service and public relations to the effect that Specialty Boards be requested by the A.M.A. to facilitate participation of its members in these emergency call services by assuring them that they may participate in such a community activity without jeopardy to specialty rating.

8. A resolution presented by the State of Mississippi was reworded and adopted to the effect that the Immediate Past Five Presidents of the A.M.A. be seated as members of the House of Delegates with right to vote. Final adoption of this idea will have to lay over until the next meeting, since it involves a change in the Constitution and By-Laws.

9. Reworded and adopted a resolution reaffirming the present policy to publish in the Journal of the A.M.A. considered discussion of

controversial medical matters submitted by member physicians. This was done specifically in order to allay the criticism of certain minority groups who allege that the editorial policy of the Journal does not allow them to publish their views concerning several areas of disagreement with A.M.A. policies.

10. The provisions for the adoption of Dues in the A.M.A. was finally adopted in the Constitution and By-Laws. The following are the essential points which will govern the questions of Dues.

A. Annual dues may be prescribed for the ensuing calendar year in an amount recommended by the Board of Trustees, and approved by the House of Delegates. Dues will include subscription to the Journal.

B. The Board of Trustees may excuse a member from payment of dues for the following reasons, provided he is fully or partially excused from payment of local dues by his component and constituent association.

a. Members on whom the payment of dues would work a financial hardship. This fact to be certified to by the secretary of the member's component society.

b. Members retired from practise.

c. Interns and residents during the first five years following their graduation, except that the time spent in military service may be excluded in calculating the five-year limit.

d. A member temporarily in the Armed Forces. Dues will be remitted and prorated Jan. 1 or July 1, following the date of the member's entrance into military service.

e. Members over 70 years of age may be excused, on request, from payment of dues regardless of local dues exemptions.

11. The Chairman of the Medical School Educational Fund, Dr. Henderson discussed at length the progress toward implementing the fund of \$500,000 announced by the Board of Trustees at the Cleveland Session last December.

He reported upon future plans to augment this fund, and announced that several substantial gifts had been received. One gift which caused prolonged applause before the House

was that of the National Womens Auxiliary, which presented Dr. Henderson with a check for \$10,000, representing approximately one fourth the income of that group for the year. Doctors over the land were urged to send in their individual contributions to this Fund, earmarking if they desire the School of their choice to receive their gift.

As pointed out by Dr. Henderson, we, in the medical profession, for two and one half years past, have devoted a great deal of time and energy to our battle against the advocates of socialized medicine. He reminded his listeners of the basic, long range of our objectives, to promote the national health through scientific activities, to foster and maintain high standards of medical practise, and to solve health problems in a manner most conducive to the public welfare. The A.M.A. now has a wide range of interests and programs based on positive objectives. One of the recent steps, of course, has been to take the initiative in attempting to help our medical schools out of their financial difficulties by the creation of the Educational Fund. It was announced that the American Medical Education Foundation was merged May 16, with the National Fund for Medical Education, of which Mr. Herbert Hoover is honorary chairman. The A.M.A. Educational Fund committee will continue its efforts to raise money from physicians, medical organizations and others in the field of medicine, while the National Fund for Medical Education will concentrate its money raising efforts on lay groups, business, industry and all other potential private donors outside the medical associations.

It was a pleasure for the Delegate to serve again in the A.M.A. House of Delegates as your representative from Arizona. It was a busy week of activity, attending the meetings of the Council on Medical Service, of which I am a member, representing the western section of the country, the meetings of the House, and as a member of the Reference Committee on Amendments to the Constitution and By-Laws of the A.M.A. Mr. Robert Carpenter, our Executive Secretary, was in attendance at the meeting, and was observed with his note book at each meeting of the House.

Respectfully submitted

Jesse D. Hamer, M.D.

ANNOUNCEMENT

Regional Meeting of the American College of Physicians

The third annual Arizona Regional Meeting of the American College of Physicians will be held in Phoenix at the Westward Ho Hotel on Saturday, September 29, 1951. Dr. Dwight L. Wilbur, Clinical Professor of Medicine at Stanford University School of Medicine will be the guest speaker and official representative of the Board of Regents of the College. The program will begin with a luncheon at 12:30 followed by the scientific program to which all physicians are cordially invited, without fee. A dinner meeting for members of the College, wives, and guests will be held in the evening at which Dr. Louis N. Katz, Chicago, President of the American Heart Association will be honored guest.

The program for the afternoon scientific session is as follows:

- 1:30 Intermittent Positive Pressure Breathing Therapy; W. Roy Hewitt, M.D., F.A.C.P., Tucson, Arizona
- 1:50 Causes of Failure in the Medical Treatment of Peptic Ulcer; Dwight L. Wilbur, M.D., F.A.C.P., Clinical Professor of Medicine, Stanford University, School of Medicine, San Francisco, California
- 2:20 Direct Venous Pressure in Chronic Heart Disease; Morris Deitchman, M.D., F.A.C.P., Veterans Administration Hospital, Phoenix, Arizona
- 2:40 Intermission
- 3:30 Dynamic Effects of Cardiac Arrhythmias Louis N. Katz, M.D., F.A.C.P., Director Cardiovascular Department, Michael Reese Hospital, Chicago, Illinois. President, American Heart Association
- 3:30 Cancer of the Lung in Patients with Chronic Pulmonary Disease; Israel Walzer, M.D., F.A.C.P., Veterans Administration Hospital, Whipple, Arizona
- 3:50 Primary Carcinoma of the Liver; Joseph Bank, M.D., F.A.C.P., Phoenix, Ariz.

It is hoped that all physicians attending the annual session of the Arizona Heart Association, and other interested physicians, will plan

to attend the afternoon scientific sessions of the College of Physicians.

Leslie R. Kober, M.D., F.A.C.P.
Governor for Arizona

PSYCHOTHERAPY MEETING

IN GENERAL MEDICINE HELD AT GRAND CANYON, ARIZONA—Oct. 3rd, 1951

This meeting is being sponsored by the Coconino County Medical Society and is primarily a regional meeting of the five Northern County Medical Societies. There will be one subject for this entire day, namely, Psychotherapy in General Medicine. It will be informal and to a large extent round table discussion following brief presentations by guest speakers.

We expect to have Dr. Hale Shirley from the Stanford University School of Medicine and Dr. Henry Cyril Schumacher who is Regional Consultant in Mental Hygiene and Psychiatry in the United States Public Health Service. Dr. Salsbury of the State Health Department will act as moderator.

Physicians who wish to come on October 2nd, may write Leo Schnur, M.D., Grand Canyon, Arizona and I will arrange for reservations. Registration will start at 10 o'clock October 3rd. This will be followed by luncheon and the program will last from 1:30 to 4:30 p.m. Arrangements are being made for a dance after the meeting.

Leo Schnur, M.D.
President, Coconino County Medical Society

ARIZONA HEART ASSOCIATION

The Arizona Heart Association is giving the following program at the Hotel Westward Ho on September 29th, 9:30 A.M. This will be followed in the afternoon by the program of the Arizona College of Physicians.

- 1) Dr. Louis Katz—"Recent Trends in Clinical Electrocardiography"
- 2) Dr. John C. Jones—"Congenital Heart Surgery"
- 3) Dr. Louis Katz—"Recent Developments in Atherosclerosis."
- 4) Dr. John C. Jones—"Mitral Valve Surgery"

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CIVILIAN MEDICAL AND DENTAL CARE FOR ACTIVE DUTY AIR FORCE PERSONNEL

The United States Air Force is responsible for the provision of medical and dental care to United States Air Force military personnel on active duty, and to their dependents in so far as facilities are available. Whenever it is feasible and practicable for Air Force personnel to receive medical care at Air Force medical installations they should do so. Conversely, Air Force medical installations provide medical and dental care to all Air Force personnel who may be assigned in the area, whether or not these personnel may be assigned to the particular Air Force Base.

Naturally it is not possible to have USAF medical installations readily accessible to our personnel in every geographical location. In those locations where we do not have such facilities, it is necessary to depend on other governmental or civilian agencies for these services. These agencies include medical and dental services of the Armed Forces (Army and Navy), and other federal agencies, such as the Veterans Administration and the United States Public Health Service. When medical and dental services of government agencies are not available, care may be obtained from civilian sources at no expense to the individual, provided such care is a necessity and an emergency. Only active duty Air Force personnel on duty, leave or informal leave (pass status) or those people stationed where no other military or federal medical installation is available may utilize civilian medical care at Air Force expense. USAF military personnel absent without official leave (AWOL) are not authorized civilian medical care, but can receive treatment at any military installation. Depends of active duty Air Force personnel are not authorized civilian medical care at Air Force expense.

All bills for services, including ambulance charges, rendered USAF military personnel by civilian physicians or medical facilities will include:

1. Full name, rank, service number and organization to which assigned for duty.
2. Duty status of patient, if known, i.e., duty, leave, or informal leave (pass).
3. Inclusive dates of treatment if hospitalized, otherwise, date and place of treatment.
4. Diagnosis.

5. Charges (itemized separately for services, drugs, x-rays, etc.).

6. A statement certifying that the bill is correct and just; that payment has not been received; that the services rendered and the medicine furnished were necessary; and that charges do not exceed those customary in the vicinity.

Payment for medical and dental service properly submitted from civilian sources to USAF military installations will be accomplished promptly after receipt of necessary authenticated vouchers. The civilian physician is advised to send the bill for services rendered directly to the Commanding Officer of the nearest Air Force Base.

SECRETARY LULL'S LETTER

Editor addresses Conference of Presidents. One of the best speeches delivered at the recent A.M.A. session in Atlantic City was entitled "An Editor Views Medicine." It was delivered before the Conference of Presidents and Other Officers of State Medical Associations by Edwin F. Abels, publisher of the Lawrence, Kansas, Outlook, and past president of the National Editorial Association.

"It has been said before, and I only repeat it, freedom in this nation is being poisoned," he told the conference which was attended by an overflow crowd. "It is sick unto death. The editors of the papers I represent have known this fact and have been concerned about it. It never occurred to them to call in the doctor to help cure this case of poisoning. Foolishly, they kept calling on the politicians, some of the very men who were mixing the libation. What a thrill it was when you men walked in, unannounced, and told the world to count you on the side of freedom, liberty, private initiative and all of the privileges and opportunities that have contributed to the greatness of this nation. Yet it was the natural thing for you to do. History tells us that yours is a profession built by men of courage, vision and greater intellect. . . .

"What America needs today, what your profession and my business need, more than any other one thing that I can call to mind, is men of courage to speak out fearlessly and courageously for what they know to be right. You did it in your advertising campaign and you inspired thousands of others to follow your example. By that campaign you won new prestige."

BOOK REVIEW

Handbook of Nutrition—2nd Edition.

Prepared under the auspices of the Council on Foods and Nutrition of the American Medical Association. Reprinted from the Journal of the AMA with additions. 7 Charts; 28 Tables; 35 Figures; 717 Pages, May 9, 1951. \$4.50. Blakiston.

This handbook includes 28 articles by 32 authors, and has 4 parts. Part I discusses proteins, fats, carbohydrates, minerals, vitamins. Part II takes up food needs of adults, infants, women during pregnancy and lactation, old age, illness. Part III treats of food imbalance, starvation, fluids, lack of vitamins and minerals. Part IV assesses American diets, plant and animal foods, emergency rations, and how to improve quality in cheap staple foods.

The book bulges with references, at least 1473, many with several sub-references. Here is an impressive array of recent research, even though much of it conflicts. Facts, or at least experiments, abound. In that lies the book's merits and defects. A busy clinician will tend to get indigestion from the very wealth of uncorrelated facts.

At times we run into interpretation of facts, not always fortunate. For example on P. 413 an author seems to say that weight alone may serve as a good criterion of nutrition. Hasn't he heard that overweight often gives the first sign of partial starvation? As well decide the value of a doubtful piece of gold by merely weighing it.

Yet in the introduction we get some hints of basic problems. We read the almost wistful admission that hucksters in advertising do more to decide food habits in American than all the doctors lumped together. Also a shy awareness that all may not be well with our food. Modern man developed until this century living almost entirely on unprocessed or slightly processed foods. But today doctors and patients alike engage in a stupendous if little noted gamble. We stake our whole future on a gamble that the human species, till almost yesterday living on unprocessed or slightly processed foods, can survive and meet all challenges on a diet of highly processed foods. Quite a tribute to the wisdom of the processors.

It may be our gamble will pay off. Perhaps it will not. For better or worse, in 1951 many prominent nutritionists in America feel that our national eating habits are not too bad. His-

torians and doctors of 2000 A. D. kindly take note.

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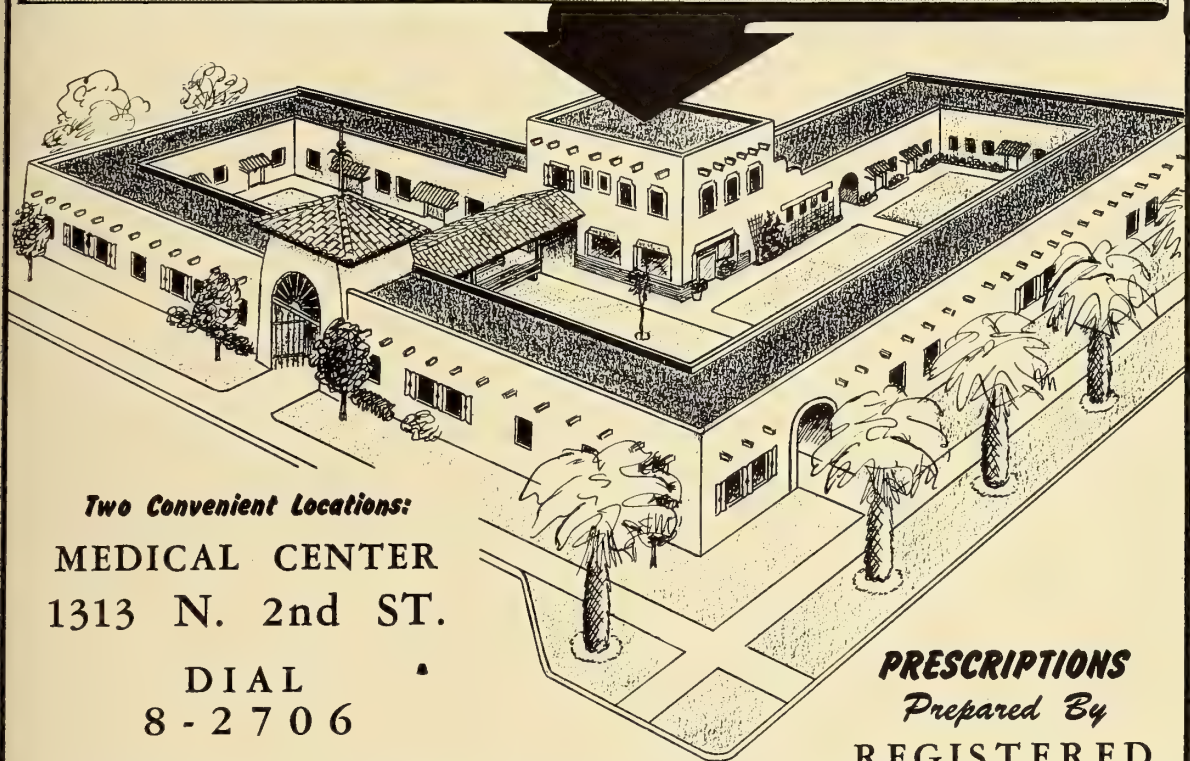
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WOMAN'S AUXILIARY

WOMEN'S AUXILIARY CONVENTION REPORT JUNE 1951

The twenty-eighth Annual Meeting of the Women's Auxiliary to the American Medical Association was held in San Francisco, June 10th to 15th, 1951. As in several past years, the attractive Hotel Haddon Hall was the scene for the women's meetings. Fifteen hundred and seventy-eight women representing their auxiliaries in all forty-eight states, the District of Columbia, and Hawaii were registered.

As this large group, delegates, members and visitors met, again and again, at round-table discussions, meetings, and luncheons, there was no question that they were well aware of the role they were expected to fill, both as individuals, and members of the community, and as doctor's wives. Perhaps Mrs. Howard P. Hamman, state president of Pennsylvania, keynoted this feeling best, when she said in her state report, "Personal freedom cannot endure without individual responsibility."

The Monday sessions were built around a series of round table discussions, of which one of the most interesting and pertinent was the one on the magazine "Today's Health." Mrs. Joseph Kelso presided at this session and Mr. Cargill who is circulation manager of the magazine spoke. He emphasized the value of the magazine in bettering the health of the American people, and pointed out that it was a great aid to the overworked doctor because it taught the patient to understand his problems and to cooperate more effectively. Inasmuch as our husbands, through national channels of the A.M.A., urge us to sponsor sales of the magazine, he pointed out it behooves all of them to buy it for their offices! The suggested techniques of selling were excellent, not only because they increased circulation, but because they carried our message to many areas where it was most needed. Thus, it was proposed, auxiliaries could present their Senators and Representatives with gift subscriptions. The same for schools, colleges, libraries and PTA groups. One state auxiliary even makes it a point to keep the magazine or health literature with our viewpoint in the stands of railroad and bus stations!

Tuesday morning was spent in the colorful opening ceremonies of a large convention, with official greetings and welcome to officers, and reports. Mrs. Herold as president read a truly inspiring report which will probably appear in a subsequent issue of this bulletin. How well she labored in our behalf was attested, not so much by her own words, but by those of state auxiliary presidents each of whom told of how Mrs. Herold had visited in her state, showing great tact and experience as she put forth our national program and guided us through individual and regional problems. Thousands of miles were spent crossing and recrossing the country in what was an arduous but compensating year.

The afternoon session was varied in its scope, with many of the Eastern and North Central Auxiliaries reading their state reports at this session. This procedure continued for three days to include the reports of all the presidents and many had to be halted before the end of their excellent reports because of the time element. The competent report of our State President, Mrs. Ben Herzberg, was read for her by Mrs. Lawrence von Pohle, and we can say with pride that for our size as a state and our membership, we stacked up well with the other states, and can rightfully boast in addition that Mrs. George Enfield's report on "Today's Health" in our State Medicine won national recognition!

During the same afternoon session, under legislation, the pitfalls inherent in many of the bills sponsored by the government were discussed. Among those to watch is Senate Bill 445 which is a Local Health Unit Bill that is very vague in its wording but delegates unrestricted power to the Surgeon General's office. Mr. Priest has improved the bill for further presentation in by Congress more clearly defining who has what powers; but the bill is still dangerous because of its back door entree of the government into the province of private medicine.

Senate Bill 337 with its Federal Aid to Education, likewise seems innocuous enough until one analyzes that one of its provisions would give up to 40% of the needed income of Medical Schools from government sources. This bill has the approval of the American Legion and the National Grange, which are usually alert to break-downs in the laissez faire system, but apparently do not seem yet aware that the joker

in this bill lies in the fact that 40% donation or grants may well make the government the single agency able to dictate all the terms for running medical schools unless again its scope and power is officially defined and limited.

There are many exhibits that we members of the auxiliary can avail ourselves of for our own, or public meetings that will further our message according to Mr. George Larson who is assistant director of the A.M.A. Scientific Exhibits. These include technical and scientific exhibits, a movie on babies, and one on nurses.

Our national President, Mrs. Arthur A. Herold, presided at the Wednesday session. Mrs. Ross P. Daniel read the touching Memorial Service. This meeting was a long one with the revisions committee report of Mrs. Eustace Allen calling forth much discussion and clarification. This was due to the fact that for the first time in history, the National A.M.A. has decided on a policy of physicians paying dues to National in order to be eligible for local and county membership. In line with this policy it was therefore necessary to make the membership of the wife contingent on the husband's compliance with the national ruling. The revisions had the benefit of full floor discussion until it was felt everyone understood and was in complete agreement. Though the proceure was tedious, the membership was impressed with how it represented democracy in action. All the revisions passed as recommended, with the one exception that the requirements for a Director were relaxed to require only that she have fulfilled a term as State President, or have held a National office or chairmanship for one year, in order to make more women eligible for this office.

Mrs. Jesse Hamer,—our Clarice—reported as National Historian and again “did us proud” as she showed her firm grasp not only of the principles for which the Auxiliary stands, but of what every state president had incorporated in her report!

The final day of the general sessions again had its note of formality with final convention reports of attendance, nomination and election of officers. These follow:

- President Mrs. Harold F. Wahlquist
Minneapolis, Minn.
- President Elect Mrs. Ralph Eusden
Long Beach, Calif.
- First Vice Pres. Mrs. Leo J. Schaefer
Salina, Kansas

- Second Vice Pres. Mrs. Mason G. Lawson
Little Rock, Ark.
- Third Vice Pres. Mrs. Herbert W. Johnson
Everett, Washington
- Fourth Vice Pres. Mrs. Jay G. Linn
Pittsburgh, Pa.
- Treasurer Mrs. George Turner
El Paso, Texas
- Constitutional Secy Mrs. Jay Emerson Noll
Port Jervis, N. Y.

Again Arizona came to the fore, as Mrs. Jesse Hamer, with tact and charm, installed the new officers, and Mrs. Rollo Packard presented the diamond-studded pin that is the insignia of this high office. Mrs. Harold Wahlquist replied feelingly, of her desire to follow in the footsteps of her predecessors, and the need for all of us individually as well as collectively to work together. Her address will likewise follow in a subsequent issue of the Bulletin, so we shall not give it here.

The Convention was inspiring for its hard work, and long hours, but the famous Boardwalk gave occasional surcease as wives and delegates thronged it, window-shopping, visiting inside the many bazaars and stores. The bracing salt air provided a nice memory for us returning to the Arizona summer time. And the hospitality of the city, with Mrs. David B. Allman, as General Chairman, surpassing herself, in the courtesy provided,—the many luncheons, and fashion show, culminating in the final ball. To her and her able committee go our thanks for a convention, not only well done, but graciously done.

Arizona's delegates to the Convention were: Mrs. Jesse Hamer, Mrs. George Enfield, and Mrs. Joseph Bank from Phoenix; Mrs. Lawrence von Pohle from Chandler and from Tucson Mrs. Jackman Pyre and Mrs. John Rupp. The above report is a composite of the reactions, notes, and impressions of these delegates.

Mrs. Joseph Bank, Editor

ATTENTION WOMAN'S AUXILIARY MEMBERS

Kindly mail the following form on a postal card or in an envelope with your CORRECT ADDRESS to Arizona Medicine, 426 Heard Bldg., 112 N. Central Avenue, Phoenix, Arizona.

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EXCHANGE OF TELEGRAMS

April 3 1951

Editor Journal of the American Medical Association

535 North Dearborn St. Chicago

My attention has been called to the President's Page in March 31 issue Journal American Medical Association. It quotes sentence from what you mistakenly call a "Current" pamphlet, describing it as "Mr. Ewing's directive" any reputable scientific periodical verifies statements before publication. Elementary check would have revealed that pamphlet was written and issued in 1945, some two years before I became Federal Security Administrator. Checking would also have revealed that this pamphlet is not being currently distributed by Federal Security Agency, and has never had remotest authority as directive. Since you profess to be a scientific magazine interested in truth I suggest you retract the statement as publicity as it was made in the first place.

Oscar R. Ewing Federal Security Administrator
Federal Security Agency Wash. D.C.

April 11, 1951

The Honorable Oscar R. Ewing
Federal Security Administrator
Federal Security Agency
Washington, D. C.

We have your telegram of April 3, protesting a reference in the Journal of the American Medical Association, to a pamphlet issued by your office titled: "Common Human Needs, an Interpretation for the Staff in Public Assistance Agencies," from which I quoted the following passage: "Social Security and public assistance programs are a basic essential for attainment of the socialized state envisaged in a democratic ideology, a way of life which so far has been realized only in slight measure."

We note your denial of responsibility for the pamphlet on the grounds that it was published in 1945 before your tenure as administrator of that office. This denial, as you request, will be duly reported in the Journal. You are correct in assuming that as reputable scientific periodical it is the habit of this Journal to verify statements before publication. The facts concerning my reference are these.

The pamphlet in question was reprinted for distribution by your office in 1949, when the public record indicates you were in charge of the Federal Security Agency, its publications

and its directives to employees. Five copies were received in the mail here last week, which indicates certain currency still. These all carry the imprint, "Government Printing Office, 1949." The fact that the report was first printed in 1945 would not seem to alter the further fact that you apparently have thought well enough of it to have it reprinted in 1949.

We would suggest that if you wish at this time to disavow the principles expressed in the pamphlet, you will wish to do so in a formal statement to Congress, for as recently as February 26 this year, it was protested on the floor of Congress as a grave misuse of taxpayers' money to disseminate wholly unamerican philosophies.

In case it was without your knowledge that your office was reprinting and distributing such Unamerican directives during your tenure, you may wish to issue a public statement disclaiming responsibility for the material. If so, we shall certainly be glad to be helpful in giving such a statement further distribution through the Journal, for the medical profession will be sincerely interested in any such action.

Elmer L. Henderson, M.D., President
American Medical Association
535 North Dearborn, Chicago

PERSONAL NOTE

Dr. Harold Wood will take leave of absence from his positions in Phoenix for a year commencing September 1, 1951, to accept an Associate Professorship in Pathology at Baylor University Medical College, Houston, Texas. His private laboratories will function as at present while he is away, and he will be available for consultation on tissue sections. Professional advice will be available to the laboratory staff through one of the local Pathologists.

NEWS ITEM

A revised catalog of motion pictures available through the Committee on Medical Motion Pictures is now available. Copies will be sent to the secretary of each county and state medical society. This catalog lists sixty-two 16mm. films, most of which are at the professional level. Fourteen of these films are suitable for showing to lay groups. Eight new films have been added. Copies are available upon request from:

Committee on Medical Motion Pictures
American Medical Association
535 N. Dearborn St., Chicago, Ill.

NATIONAL EMERGENCY

The Joint Committee on Medical Education in Time of National Emergency, in cooperation with representatives of the Surgeons General of the branches of the Armed Forces and of the Public Health Service, the Selective Service System, the Veterans Administration, and the National Security Resources Board, has for the past six months been studying and has reported to the N.S.R.B., means for meeting the needs of the country for doctors in an acute and prolonged emergency through the thorough training of as large a number of well selected physicians as possible. The Joint Committee came into being as the result of studies which each organization has been making since the last war. The Committee has full confidence that thus a number of marked deficiencies in the training and utilization of doctors during World War II will be avoided in the present emergency. It has prepared a statement for the N.S.R.B. which is attached to the present testimony.

On the basis of this study the Joint Committee is desirous of registering approval of H.R.2811 as contrasted with H.R.1752 and S.1 and S.1 amended.

The Joint Committee is especially pleased by the omission from H.R.2811 of the provision for the temporary deferment for study or research of 75,000 students annually upon completion of an initial four to six months basic training, which was included in sub-section d, section 6, page 9 of H.R.1752. We commend strongly the inclusion instead of the new amendment to sub-section h, section 6, which on pages 14-15 of H.R.2811 states as follows:

"The President is authorized, under such rules and regulations as he may prescribe, to provide for the deferment from training and service in the Armed Forces, or from training in the National Security Training Corps of any or all categories of persons—whose activity in study, research, or medical, scientific or other endeavors is found to be necessary to the maintenance of the national health, safety, or interest: *Provided*, That no person within any such category shall be deferred except upon the basis of his individual status: *Provided further*, That persons

who are or may be deferred under the provisions of this section because of their activity as students, shall remain liable for training and service in the Armed Forces or for training in the National Security Training Corps under the provisions of section 4-(d) of this Act until the thirty-fifth anniversary of the date of their birth."

Inclusion in H.R.2811 of the above new wording of sub-section 2, section 6, to permit the President to authorize deferment of students for study and later military service has the following advantages over sub-section d, section 6 in H.R.1752:

1. If activated, it will avoid a period of double duty for students of medicine and other professions. H.R.1752 provided that the temporary deferment of 75,000 students annually should be operative only until June 30, 1954—a three year period. After 1954 all men reaching the age of 18 would serve on active training and service in the armed forces for a period of 27 consecutive months, in which would be included, at the beginning, a four months period of basic training. After this period of military service, students would then be able to go to college, subsequently to medical school. After graduation from medical school, it appears altogether probable that the requirements of the armed forces of this country would necessitate a second period service, this time as physicians, for all physically qualified medical school graduates. The same would apply for dentist, engineers and other professions. This kind of selective obligation to double duty of certain groups of society, as contrasted with the rest of the age group, is undemocratic, wasteful, and would probably tend to discourage people from entering the study of medicine and other professions.

2. It will avoid limitation of deferment to a specified number, 75,000, which in practice might well work out to be in insufficient number. The Joint Committee is on record as recommending deferment of a pool of college students of high general competence for each year, from which would be selected medical students, dental students, physics students, engineers, linguistic and cultural experts, etc. We recommend the procedure reported by the six Scientific Advisory Committees—the Trytten Report to the National Director of Selective Service System, dated December 1, 1950, in which it is recommended that a student whose aptitude is such

Statement of Dr. Stockton Kimball, Chairman, Joint Committee on Medical Education in Time of National Emergency. Filed with House Armed Services Committee in regard to H.R.2811 (War Manpower Bill).

Reprinted from The A.M.A. Washington Office.

that it is deemed necessary that his preprofessional or professional training be continued in order to increase his potential value to the national health, safety or interest, be placed in a classification or category that will permit him to continue his education. We believe that a student qualifying for such classification should be so classified before or at the time he reaches the age for induction and that his basic military training and service be postponed until his specialized education is complete, or until he ceases to pursue his education satisfactorily. This procedure would be in accordance with sub-section h, section 6 of H.R.2811.

In the plan suggested by the six Scientific Advisory Committees, the scores on classification tests and the level of past achievement used as the basis for this classification could be readjusted periodically to provide for a larger or smaller pool of students, depending on the Nation's need for manpower in various categories. The advantage of such a plan is that the selection of students remains in the hands of those most fitted to exercise these functions—the colleges and the universities themselves. Similarly the selection of medical students should remain in the hands of the medical schools. It was clearly demonstrated in World War II that selection of medical students by representatives of the armed forces, rather than by the individual medical schools, led to the selection into medical schools of many less well qualified students.

3. It will avoid interruption of studies for a period of four to six months of basic training. Such interruption would result in a loss of valuable time, a loss that, because of schedule adjustments in the colleges might exceed by several months, the actual period of training. This period, whatever its length, represents a deviation in time and effort which might better be spent in the educational program. Further, if students should be required to be inducted and to go through basic training before discovering whether they are to continue their studies, it is likely that the uncertainty of their future course would seriously distract many of them from their work for at least a year preceding their induction. It will be possible for certain of these students to enroll in an R.O.T.C. program and therefore to obtain basic military training during their period in college, or in summer vacations.

4. This Bill obligates such deferred students to later training service in the Armed Forces, or for training in the National Security Training Corps until the thirty-fifth anniversary of the date of their birth, thus insuring that they will receive *deferment* for education, not *exemption* from military service.

The Joint Committee is in favor of the provision for an R.O.T.C. or similar Corps, as provided in sub-section d, section 6 amended in H.R.2811. We do not favor the provision adding a period of one year to the obligated active commissioned service of any person who has agreed to perform such obligatory service in return for financial assistance while attending a civilian college. We do not believe that students receiving such aid should be obligated for service over and above that expected of their fellows.

We are concerned that under H.R. 2811, all able-bodied men, by virtue of assignment to the reserve components of the armed forces, after completion of their initial service, will be subject to the control of the military for a long period of years.

We have been impressed by the recommendation presented to your committee by the Scientific Manpower Advisory Committee of the National Security Resources Board that a National Scientific Personnel Board or some similar agency be established. We strongly concur with that Committee's observation that, following a program of Universal Military Training and Service, there will gradually accumulate an entire generation of reservists and that some effective machinery for insuring that these individuals will serve in the manner which contributes most to the strength of the nation should be devised. A National Scientific Personnel Board or similar agency is vitally needed if we are to secure the proper distribution of reserves with special training between civilian and military needs.

MEETING NOTICE

The Third Annual Meeting of the SOUTHWESTERN SURGICAL CONGRESS will be held at the Hotel Jefferson, St. Louis, Missouri, on the dates of September 24 through 26, 1951. Reservations may be secured by writing direct to the hotel. Registration will begin at 12:00 Noon on Sunday, September 23, and at 8:00 A.M. on each succeeding day. (There will be a \$10.00 Registration Fee for **non-members** of the Southwestern Surgical Congress, only.)

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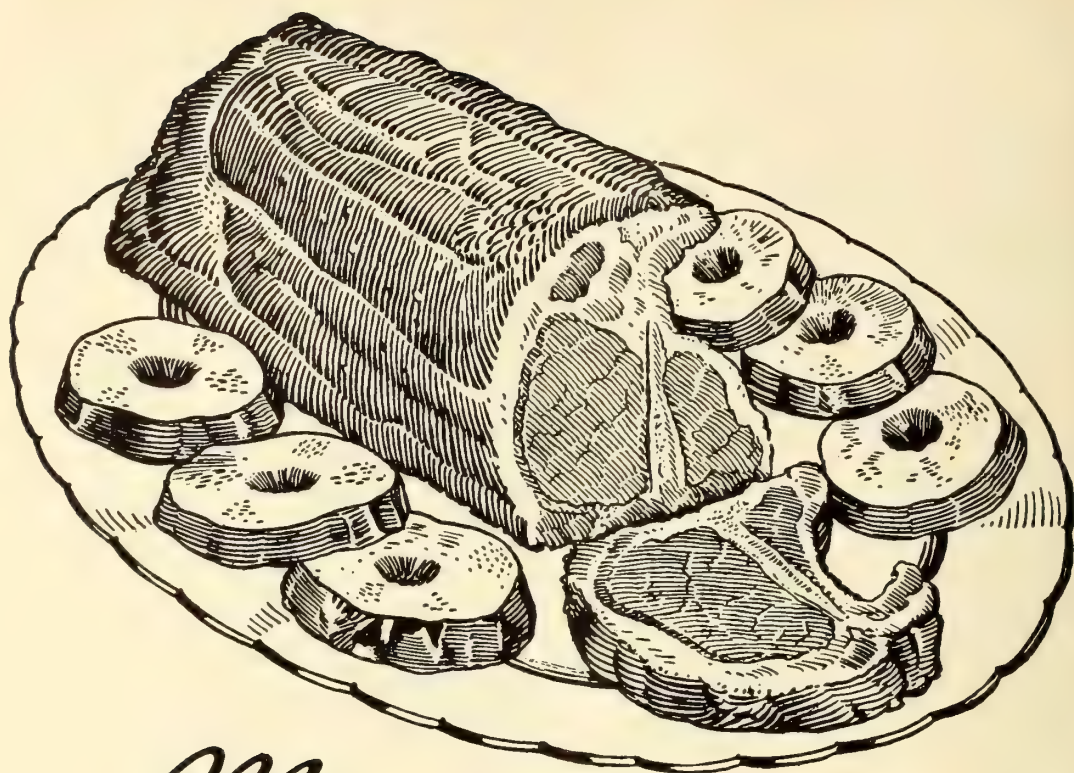
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ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 9



SEPTEMBER, 1951

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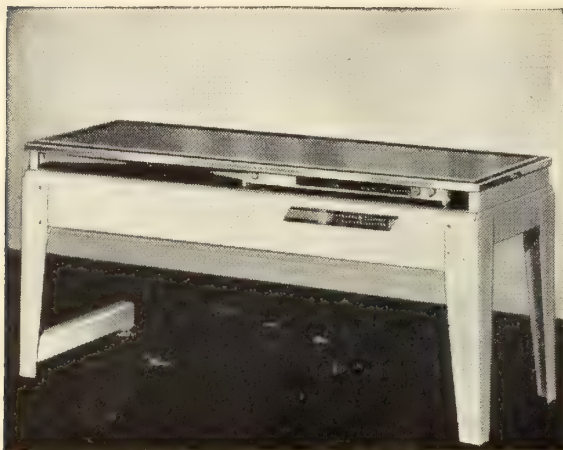
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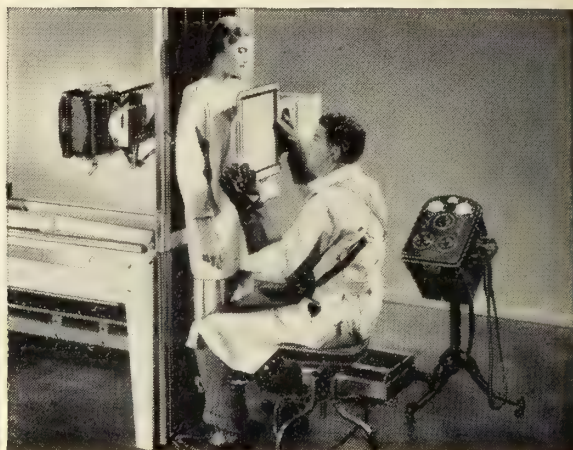


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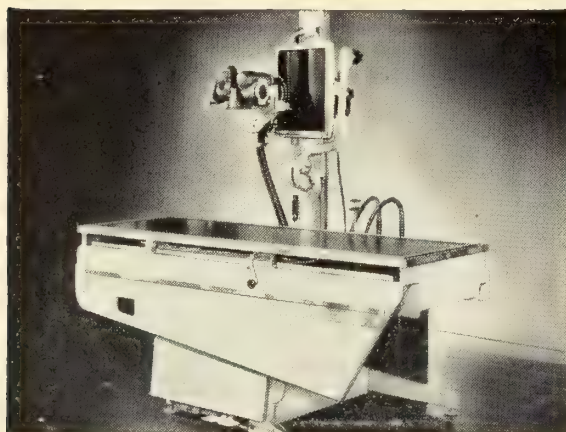
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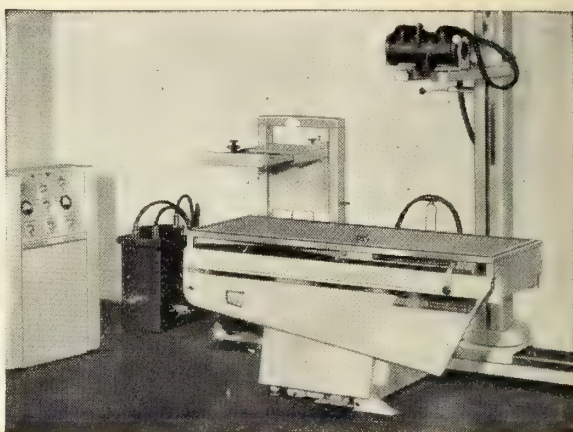
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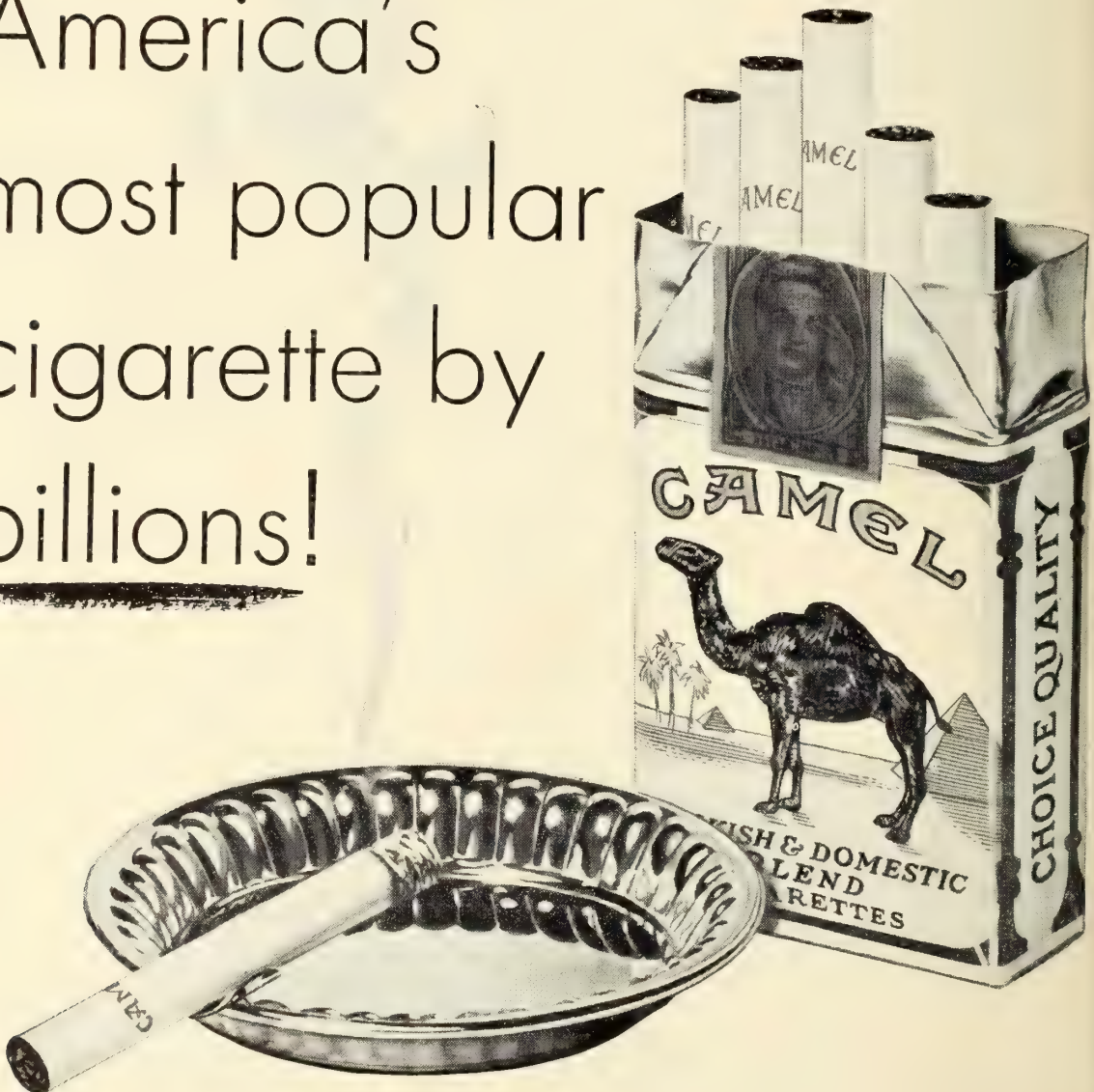
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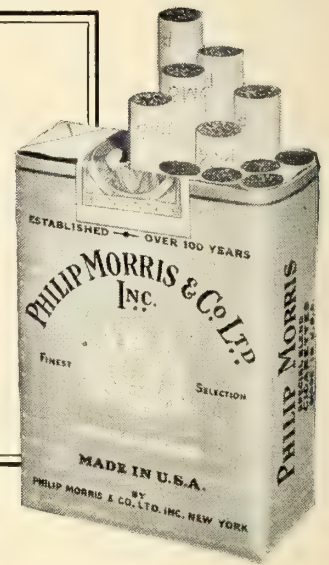
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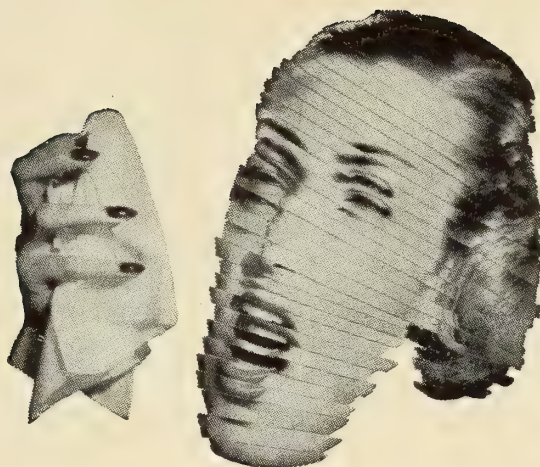
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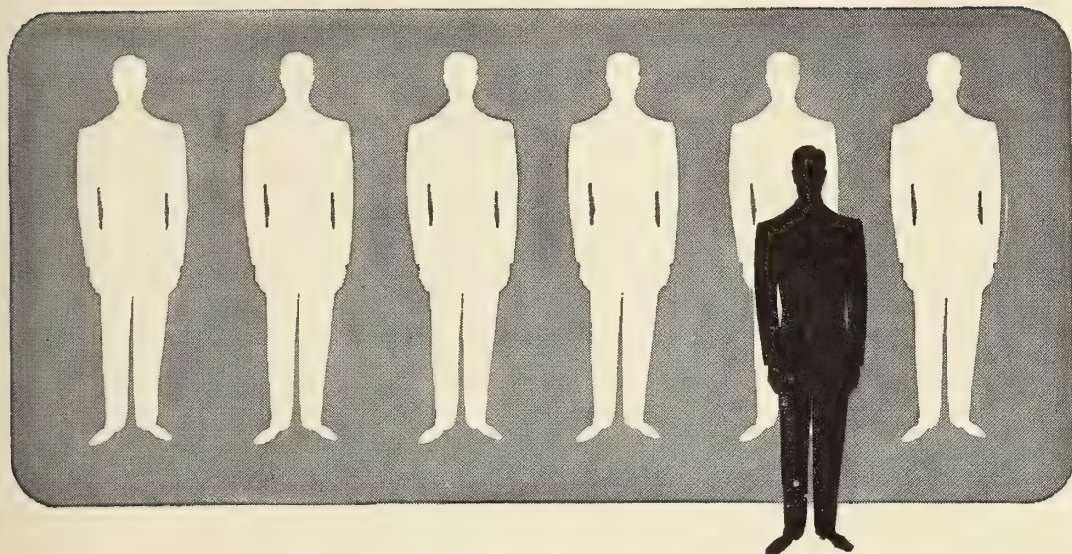


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Hamblen, E. C.: Some Aspects
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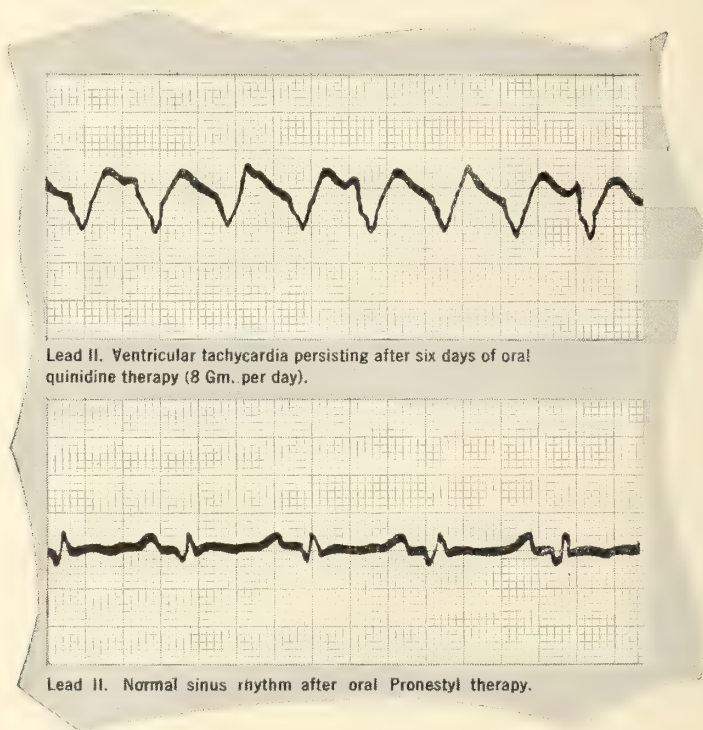
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Head Pain as a Diagnostic Lead

Frequently the presence of head pain is overlooked. The physician learns of it only if he has made an effort to elicit the information. Since the etiology of the pain is the basis of rational management, the patient should be warned against taking medication before diagnosis is made.

Friedman¹ deplores the tendency to call any chronic recurring headache migraine. Careful history-taking and full physical and neurological examinations are essential for accurate diagnosis. A good starting point is a description of the headache — its character, laterality, frequency and intensity.²

The following chart gives briefly the primary diagnostic leads and treatment for the most common types of headache.

Etiology of Headache	Primary Diagnostic Data	Primary Therapy
Inflammatory e.g., Meningitis Abscess	Inflammation of intracranial structures; fever; leucocytosis; bacteriologic diag.	Specific: sulfonamides and antibiotics. Symptomatic: analgesics.
Tumor	Pain varies as spinal press. changes; skull X-ray.	Specific: surgery. Symptomatic: analgesics &/or hypnotics.
Sinusitis	Sinus congestion and infection; cloudy X-ray.	Specific: antibiotics and drainage. Symptomatic: analgesics.
Hypertensive	Hypertension present but pain not related to b.p. level; Dihydroergotamine relieves pain.	General hypertention therapy; sedation. Symptomatic: analgesics.
Migraine & other vascular headaches	Headache: recurrent, intense, throbbing. No organic causation; migraine in family; patient: energetic, perfectionist. Visual prodromata; g.i. upset during headache.	To abort attack: oral ergotamine plus caffeine. General: adjustment to minimize nervous stress.

Data here tabulated is from: Wolf, G., Jr.,³ and Friedman, A. P.⁴

Cecil⁵ ranks vascular headaches, e.g., migraine and tension headaches, as the most commonly encountered of all. Because of their functional nature and usual recurrence at frequent intervals, they present a long-term therapeutic problem.

Therapy is conducted along two lines:

1) *Psychotherapy to reduce the frequency of attacks. This consists mainly of advice on emotional adjustment to stressful situations and guidance toward a good balance between work and relaxation.*

2) *Treatment of the distressing attack to prevent the usual period of incapacitation. Many investigators have reported that ergotamine preparations are effective for relief of the acute migraine attack in 80% of cases.^{1,6} The drug is given immediately when an attack is approaching and dosage adjusted to the needs of the individual.*

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Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 9



SEPTEMBER, 1951

ORIGINAL ARTICLES

THE CLINICAL APPLICATION OF CORTISONE AND ACTH IN ARTHRITIS AND RELATED CONDITIONS: METHODS AND PROBLEMS

PART II: SIDE-EFFECTS, COMPLICATIONS, CONTRAINDICATIONS,
PRECAUTIONS AND CONCLUSIONS

By

Otto Steinbrocker, M.D., Mortimer E. Ehrlich, M.D., Murray Silver, M.D.,
William Sicher, M.D., Sidney Berkowitz, M.D., Solomon Carp, M.D.,
and Harold Feinstein, M.D.

From the Arthritis Department of the Hospital for Joint Diseases and
Lenox Hill Hospital, New York, N. Y.

Presented by the senior author before the Arizona Medical Association,
May 1st and 2nd, 1951

SIDE-EFFECTS AND COMPLICATIONS WITH ACTH AND CORTISONE

In the course of both short- and long-term administration of cortisone and ACTH in 140 cases with arthritis and allied musculoskeletal conditions, the clinical observations previously discussed also included a variety of side-actions and complications. A presentation of the consequences of using these remarkable compounds must include the undesirable reactions as well as the usual, and often striking, benefits.⁽¹³⁾ In this discussion of side-effects and complications, we have reserved the term "complications" for those pathologic states developing during the administration of ACTH and cortisone (without necessarily proving a causal relationship), which are not reversible after cessation of therapy, or for those reactions which constitute a threat to the patient's well-being or survival.

The side-effects and complications which appeared during the administration of the substances to our first 128 patients are listed in Table 7. The large number of reactions noted is due to multiple incidents in some cases.

These benign or untoward effects occurred in about 40% of the patients in our series. Approximately 90% of these side-actions were temporary, quickly reversible on discontinuance of therapy, or of no clinical importance.

Glycosuria occurred in 18 cases. It remained after interruption of the hormone in only two, and it is likely that they were patients with latent diabetes activated by the use of ACTH and cortisone. The glycosuria was transient in the other 16 cases and disappeared either following withdrawal of treatment, or during continued administration. In some patients the glycosuria was not associated with a hyperglycemia and it seemed to arise from a lowered renal threshold.

Edema was seen in 16 cases. This required intervention with mercurial diuretics in only 8. In 2 patients cessation of therapy was imposed by the increasing edema. Occasionally eccentric swelling of a part, without peripheral pitting, is the only sign of invisible edema in patients gaining weight rapidly.

Rounding of facial and bodily contours was

encountered 12 times. This usually unimportant side-effect was seen most clearly and frequently in those patients on long-term programs.

The cutaneous side-effects included hirsutism, acneform lesions, diffuse or circumscribed miscellaneous eruptions (particularly erythematous), purpuric eruptions, striae and, in one patient, pigmentation of the nails. These integumental reactions occurred in 30 cases.

Menstrual disturbances were noted in 4 cases, with prolonged amenorrhea in 2. Impotence was reported by two male patients. However, in another male and in one female there was increased libido.

Seven patients developed gastro-intestinal disorders, only one of which was serious. This was in a case on ACTH who suffered a perforation of his duodenal ulcer before admission to our service. Two of the patients receiving the early preparations of ACTH complained of abdominal cramps and four on cortisone acquired stubborn constipation.

Psychic disturbances appeared in 24 cases. Fourteen patients became somewhat euphoric and four complained of insomnia. Although 7 patients exhibited psychotic symptoms at one time or another, these effects were temporary and disappeared promptly on cessation of therapy.

Sixteen instances of untoward cardiovascular and peripheral vascular manifestations were seen in 15 patients. Five of these developed transient hypertension, which did not require interruption of therapy. One patient had symptoms of coronary insufficiency and mild congestive failure during the use of cortisone, but he had experienced similar episodes before receiving this compound.

Seven patients developed thrombophlebitis. Unilateral edema of an extremity, with suppressed external signs of local inflammation, may be the first ominous evidence of this complication. Bilateral femoral arterial occlusion occurred in one case. One patient developed a hemiplegia which cleared right after cessation of cortisone administration. Soon after its resumption, owing to a severe recurrence of polyarthritides, signs of cerebral thrombosis and diffuse encephalopathy became evident.

All but one of those presenting vascular complications were in their 6th to 8th decade of life. It is, therefore, quite possible that some of these serious developments were not causally

related to the administration of ACTH or cortisone, but were coincidental developments. Their frequency in this series, however, seems to exceed the ordinary expectancy of these events. This fact together with the reported changes in blood coagulation time⁽¹⁵⁾ during the use of these compounds leads us to view these complications with some concern, while awaiting the accumulation of sufficient data to warrant more reliable interpretation.

Six patients exhibited signs and symptoms of a variety of neuropathies. Two cases developed a paresis of the extensor muscles of the 3rd and 4th fingers of one hand, while two others complained of paresthesias in the hands and feet. Another patient felt annoying symptoms along the course of one ulnar nerve. Paresthesias cleared when dosage schedules were lowered or discontinued. The sixth patient, not of particularly neurotic temperament, noted a gradual diminution of the sense of smell after 2 months of cortisone administration. The compound has been continued for a total of 7 months now with an apparently complete anosmia and some disturbance of taste. Here again, the frequency of neuropathies seems to exceed ordinary expectancy even in patients with rheumatoid arthritis.

Severe weakness and asthenia developed in three patients during treatment. Similar "withdrawal" symptoms occurred after discontinuance of cortisone in two cases, and ACTH in another.

That ACTH and cortisone are capable of producing a negative calcium balance is well known. Decalcification of bone, or aggravation of pre-existing osteoporosis to an extent sufficient to lead to specific complications occurred in two of our patients. One with severe peripheral rheumatoid arthritis was doing very well on a prolonged maintenance program of cortisone. No spinal symptoms had been noted, although a mild pre-existent osteoporosis was seen. She suddenly developed acute dorsolumbar back pain, and a compression fracture of the 11th dorsal vertebra was found. Another patient was recovering from a "frozen shoulder" after an initial course of cortisone in the hospital. She sustained a fracture of the surgical neck of the humerus after five weeks of maintenance therapy at home. In her own words: "I brushed the door-frame with my arm while passing through a doorway." Pain was not severe, although it seemed out of proportion to the extent of the

injury. Roentgenograms revealed the unexpected fracture as well as increased osteoporosis of the upper end of the humerus.

CONTRAINDICATIONS TO ACTH AND CORTISONE

The prevention of side-effects and complications depends on a constant awareness of the tendency of these compounds toward a variety of undesirable effects. Some absolute and relative contraindications to their use now are recognized. These are listed:

Contraindications to ACTH and Cortisone

Extensive old tuberculous lesions; any early ones
Cardiac failure
Severe diabetes, difficult to control
Psychotic episodes.
Severe psychoneurosis
Severe hypertension
Infectious disease and suppuration
Malaria
Severe osteoporosis
Administered cautiously (if at all) in:
Diabetes mellitus
Mild hypertension
Cardiovascular disease, compensated
Severe varicosities, phlebothrombosis
Obliterative arterial disease
Osteoporosis, post-menopausal and senile
Neurosis

PRECAUTIONS IN ADMINISTERING ACTH AND CORTISONE

Our own observations have taught us that continual alertness and the avoidance of any sense of false security after a short experience without incident are essential to the use of these substances with the greatest safety. A complete history as well as thorough physical, laboratory, and roentgenographic evaluation of each patient's pretreatment condition is mandatory. We have learned that special attention must be given to the cardiovascular status, past tendency toward intravascular clotting, familial or personal history of diabetes mellitus, emotional instability, and any demineralization of bone. While Patients are under treatment, they must be followed closely and seen regularly as these compounds may greatly alter their reactivity to any purely coincidental intercurrent event. In that way any abnormalities possibly arising from the use of these materials may be detected early. The presence of relative contra-indications to the use of these compounds must be weighed carefully against their expected benefit in each case.

The fact that we have reported no instances of marked hypopotassemia (2, 12) may be due in part to the fact that our patients received supplemental potassium throughout therapy. Body weight, blood pressure readings, general physical and psychic assessments and other observations were made at frequent intervals, as outlined in our routine in a previous chapter.

The ability of these hormones to produce a wide variety of actions other than the useful therapeutic effects makes it necessary to administer them with due caution. It is desirable to discuss the matter tactfully with the patient or relative, and thereby share some of the responsibility involved. Accordingly, we employ the following physical and psychologic safeguards:

Special Precautions with ACTH and Cortisone

1. Hospitalization recommended for initial period.
Imperative for elderly patients and those with coincidental disease.
2. A signed release, but no longer required by us.
3. Explanation of suppressive effects (not cure);
Probably prolonged maintenance, particularly in chronic disease
4. Costs during initial period and for maintenance, frankly estimated for drugs, tests, and services.
5. Side-effects discussed with patient:
Benign
Undesirable
Complications
6. In elderly patients especially, note and re-check of:
Glycosuria and hyperglycemia
Cardiovascular competence
Varicosities
Peripheral pulses
Emotional deviations
Demineralization

COMBINED THERAPY WITH ACTH AND CORTISONE

To prevent or counteract some of the undesirable reactions to the administration of these compounds a number of therapeutic complements are being employed. Some of these are intended to correct deficiencies associated with the use of these new drugs, others to enhance control of symptoms and in that way possibly to reduce the amount of the substance required, or perhaps even to replace it. Among those utilized, or under study, are:

*Some Therapeutic Complements Used with
ACTH and Cortisone Compensatory*

Potassium chloride

Estrogens

Androgens

Thyroid extract

Dicumarol

Synergistic

Vitamin concentrates

(ascorbic acid)

Analgesics (salicylates, codeine, etc.)

Gold salts

Intermediate steroids

Physical modalities

The value of some of these agents is controversial. KCI medication generally is included to minimize any tendency toward hypopotassemia, but its place is not unanimously conceded. The use of androgens and estrogens in the prevention of demineralization is still under study. When introduced for this purpose, the methods of Albright and Reifenstein are followed with regard to dosage, route and intervals.(16) Certainly, females already subject to menopausal symptoms, or those suffering from such newly precipitated or aggravated complaints during therapy with ACTH or cortisone, should receive supplementary sex hormones to control those particular features.

Thyroid extract is under study in those patients receiving ACTH and cortisone who develop a type of obesity and other features suggestive of hypothyroidism. The additive value of this substance has not been clearly demonstrated as yet.

Dicumarol is being employed in patients developing vascular complications. When, for good reasons, ACTH or cortisone is to be utilized in individuals known to have suffered thrombovascular, or occlusive episodes, the addition of the anti-coagulant is justified.

The introduction of ascorbic acid in the management program of patients getting the new compounds has not produced any recognizable benefits in our limited experience with this innovation. Gold salts are being combined with cortisone in simultaneous and other techniques but, up to the present time at least, it appears that chrysotherapy adds no advantage over the use of either agent alone.(2,17) This may not prove to be true of ACTH, although too limited evidence of combined effectiveness is available to date for any conclusions.(18)

Analgesics, usually salicylates and/or codeine, frequently are prescribed in ordinarily adequate doses before raising the amount of ACTH or cortisone during the maintenance period. Sometimes the need for increasing the maintenance level of the latter compounds appears to be postponed for small or long intervals. Heat modalities are apt to provide their ordinary temporary palliation and help to tide patients over a mild period of transient "rebound symptoms." The use of suitable exercises, with due caution to avoid strain, probably constitutes the most helpful physiotherapeutic measure. Intermediate steroids, such as pregnenolone and actoxy-pregnenolone have failed in our limited experience to provide any impressive complementary or substitutive action.

DISCUSSION

ACTH and cortisone have amply confirmed the observations of Hench and his coworkers that these compounds are the most potent suppressants of the features of rheumatoid arthritis by their effects on the clinical and laboratory signs of this disease. We have noted similar suppressive action in other musculoskeletal conditions, some of which have been reported by them and others. The striking control of locomotor symptoms provided by these substances must be balanced by the knowledge of the frequently temporary nature of their benefits, as well as their potential for producing annoying and sometimes serious reactions. The widespread influence of these powerful hormones on the metabolic processes of the body probably accounts for the diversity of side-effects and complications which may accompany their therapeutic activity. The clinical versatility of these compounds is evidenced by the list of symptom-producing mechanisms which respond to their use. These include inflammatory processes as in rheumatoid arthritis; metabolic disturbances as in gout; degenerative disorders as in degenerative arthritis, irritative and traumatic reactions as in peri-arthritis and in calcific tendonitis; and, apparently, neurovascular mechanisms as in the shoulder-hand syndrome.

The predominant clinical effects of ACTH and cortisone on this wide spectrum of pathogenetic processes in musculoskeletal disorders may be classified as anti-inflammatory, analgesic, antipyretic, anti-allergic, anti-fibroblastic and altered tissue membrane permeability. The primary questions that repeatedly arise while ad-

ministering the preparations are: Can all of these varied clinical consequences be explained by a single form of chemico-physiologic action affecting the reactivity of the connective tissue of supportive structures to any of a host of insulting agents; or, do they reflect a wide multiplicity of actions of the hormones in various forms of pathologic physiology? Are the observed effects due to a peripheral action alone, or are associated central, visceral and peripheral responses involved in the outcome? These questions bearing on the more exact manner in which these compounds control symptoms have not been clarified as yet.

Whatever the answers to these questions may prove to be, our limited experience suggests that the clinical application of ACTH and cortisone to musculoskeletal disorders may be classified practically from a broad therapeutic standpoint, according to the special considerations involved, into three major groups:

Acute Rheumatic and Locomotor conditions responsive to ACTH and Cortisone:

- Acute rheumatic fever
- Acute calcific tendonitis and bursitis
- Acute gout (colchicine-resistant)
- Collagen diseases (early)
 - Lupus erythematosus, dermatomyositis, scleroderma, periarteritis nodosa.

Chronic, relatively self-limiting:

- Reflex dystrophy (including shoulder-hand syndrome)
- Periarthritis of the shoulder
- Chronic calcific tendonitis and bursitis (?)

Chronic Progressive:

- Rheumatoid arthritis
- Rheumatoid-like arthropathies
 - Ankylosing spondylitis, psoriatic, etc.
- Chronic collagen diseases
- Degenerative arthritis

In the acute processes enumerated, ACTH and cortisone have produced impressive benefits. Their effectiveness has been studied so far on a rather limited investigative basis. In such serious diseases as rheumatic fever and the collagen complexes, they certainly merit a more thorough trial. In the others on our list of acute disturbances, colchicine-resistant gout and acute tendonitis and bursitis, the need for only short-term therapy makes their use worthy of more extensive study.

These new substances may make a helpful place for themselves in some stubborn conditions

which are relatively self-limiting, such as peri-arthritis and reflex dystrophy. In these, the prompt relief of discomfort and the shortening of the clinical course would be worthy contributions, if borne out in larger series. Administration of the new hormones here for relatively short periods probably avoids some of the ill-effects of long-term therapy.

In the last group, the chronic progressive conditions, therapy with ACTH and cortisone requires long-term administration, for an indefinite time. It is in these diseases, for which the indications usually are most compelling, that the role of ACTH and cortisone as therapeutic agents creates the most questions and problems regarding their adequacy and possible hazards.

The observations made here and those presented in the current literature naturally reflect the discernable responses and reactions during the comparatively short time that ACTH and cortisone have been available. It is quite likely that, as further information is collected on the clinical behavior and the possible pathologic effects of these compounds, our understanding of their proper and efficient application in investigation and therapy will continue to be augmented. Obviously, a balanced evaluation of the place that ACTH and cortisone may assume in our medical resources cannot be made until we have acquired this fuller knowledge of the range and circumstances of the responses and the reactions they may produce. Until then, the selective and cautious use of these substances in rheumatoid arthritis, in rheumatoid-like diseases, and in certain other acute and refractory conditions, is warranted after a mutual understanding of the factors involved, as well as the alert and meticulous management required.

The isolation of compound E undoubtedly is one of the great biochemical achievements of our day, opening a new era in that phase of medicine. The application of cortisone and ACTH to rheumatoid disease constitutes an epochal clinical contribution with limitless prospects for new lines of research and practical usefulness. These developments already have inspired the most widespread and intensive interest and investigation of the rheumatic disorders in the history of medicine. Methods of applying these new hormones by the most effective and satisfactory techniques are under wide study. It is no disparagement to state that great

efforts are being directed to the discovery of substances with "cortisone-like" or "ACTH-like" properties, yet free of the tendency of these compounds toward undesirable reactions, or to find some way of combining them simultaneously with another agent toward the same ends. It is to be hoped these objectives soon will be achieved, in one way or another, so that the great advantages of ACTH and cortisone may be utilized to the fullest.

SUMMARY AND CONCLUSION

- 1. ACTH and cortisone have produced the most rapid and effective reversal of symptoms and signs in our series of 72 patients with rheumatoid arthritis and in 27 with rheumatoid-like articular diseases.
- 2. Almost all cases of rheumatoid arthritis and rheumatoid-like arthropathies responded initially to some degree and the greater majority retained their improvement on maintenance therapy. With prolonged treatment, a small but gradually increasing number became less responsive, or developed undesirable side-effects or complications.
- 3. In our small series of twelve cases of degenerative arthritis of the hip, relief of pain and improvement in coordinated movements were produced in nine, although increased motion at

the hip occurred in only two of these. As in rheumatoid arthritis, indefinite periods of maintenance therapy have been required to sustain beneficial effects. The trend of response has been favorable in this small group which, however, is too meagre for final deductions at this time.

- 4. In self-limiting, non-rheumatoid locomotor disorders, such as peri arthritis of the shoulder (frozen shoulder) and reflex dystrophy (shoulder-hand syndrome) pain-relief and recovery of motion were impressive in most of the cases receiving cortisone or ACTH. Some of these patients retained their benefit without relapse after relatively short maintenance periods. Application of the new compounds to these self-limiting conditions, therefore, warrants further investigation.
- 5. Somewhat less than 1/3 of the patients in our series developed side-effects or untoward reactions. About 90% of these incidents were of no clinical importance. The vascular complications, the fractures, the psychoses and the neuropathies were the most troublesome and most often necessitated interruption of therapy.
- 6. Insufficient time has elapsed to properly evaluate the full potential of cortisone and ACTH for beneficial responses and undesirable

TABLE 7
Side-Effects and Complications of ACTH and Cortisone in 128 cases during Short- and Long-Term Administration

<u>METABOLIC</u>		<u>PSYCHIC ABNORMALITIES</u>	
Glycosuria	18	Euphoria	14
(transient in 16)			
Edema (peripheral)	16	Psychotic symptoms	7
Rounding of face and body	12	Insomnia	4
<u>CUTANEOUS</u>		<u>CARDIOVASCULAR</u>	
Hirsutism	9	Hypertension (transient)	5
Acne	8	Congestive failure	1
Miscellaneous	6	Coronary insuff.	1
Purpuric eruptions	4	Hemiplegia (transient)	1
Striae	2	Peripheral arterial occlusion	1
Pigmentation of nails	1	Thrombophlebitis	7
<u>MENSTRUAL DISORDERS</u>		<u>NEUROPATHIC</u>	
	4		6
<u>GASTROINTESTINAL</u>		<u>SKELETAL (Osteoporosis)</u>	
Perforation of ulcer (duod.)	1	Vertebral compression	1
Constipation	4	Fracture	1
Abdominal cramps (ACTH)	2		

reactions, particularly in relation to long-term administration in chronic, musculoskeletal disease. A balanced final appraisal of their role as practical therapeutic agents, therefore, must await further data on the range of clinical effects and possible pathologic changes produced by these substances in larger groups of cases during longer periods of observation.

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BASIC SCIENCE SEMINAR

THE PHARMACOLOGY OF ACTH AND CORTISONE

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I. INTRODUCTION

Published reports of clinical and experimental work dealing with ACTH and Cortisone have reached an almost overwhelming volume in recent months. It is hoped that this paper may be of some assistance in the task of keeping abreast of developments in this rapidly expanding field. However, a special attempt will be made to adhere chiefly to basic concepts rather than to discuss the clinical application of these hormones.

II. HISTORICAL SKETCH: DISCOVERY, DEVELOPMENT AND ISOLATION OF ACTH AND CORTISONE

It is just one hundred years ago that Thomas Addison first classically described the disease syndrome which results from the destruction or nonfunction of the adrenal gland in the human being. Thus, he noted the pigmentation, asthenia, and anorexia characteristic of the syndrome, and was aware of the extreme ease with which these patients became suddenly and critically

ill, and, in fact, often died from minor infections and stresses of various types.

The adrenal cortex is the last of the ductless glands to yield its secrets to the investigator. As for the adrenocorticotrophic (ACTH) hormone, it was Evans (1) who twenty-five years ago first reported that a pituitary extract prevented the atrophy of the adrenal gland which results from the removal of the pituitary gland in animals. Fifteen years of bioassay followed and until a quantitative method of bioassay for ACTH was achieved by Li and workers, and Sayers and workers in 1943 it was not possible for physiologists to study the effect of ACTH stimulation on the adrenal gland. Even more practical methods were found for performing the bioassay in the Armour Laboratories enabling large scale production of purified ACTH. Clinical use of their preparation in man to a large extent was first studied by Thorn (2) and Albright (3) and their associates in 1947.

It was during the last decade that increasingly more potent adrenal cortical extracts were being prepared. After five years of work attempting to extract adrenocortical hormones, Mason, Meyers, and Kendall isolated Compound E in 1935 (4). However, it was not until 1945 that the first large sample was obtained, and when given to patients who had Addison's disease it was found to be of little value. Interest in the hormones of the adrenal cortex sank to a very low level, and there was no assurance that large-scale production of Compound E was worthwhile.

In April, 1948, Sarett (5) discovered an improved method to synthesize Compound E, thus, raising the final yield nearly a hundred-fold. When a few grams were on hand, a conference was called between Merck & Company, Inc., and a group of clinicians to consider how the material should be used. It was at this meeting that Doctors Hench (6) and Kendall attempted to state a rationale for the use of Compound E in rheumatoid arthritis. As early as 1929 and 1931 Doctor Hench made two observations about rheumatoid arthritis which led him to believe that this disease was potentially reversible. He noted that pregnancy and jaundice in the female, and jaundice in the male who had rheumatoid arthritis were temporarily relieved. A bisexual hormone was suspected. It was also noted that pregnancy and jaundice temporarily relieved such non-rheumatic conditions as hay-fever, asthma, sensitivity to egg, migraine, and psoriasis. Hence, it was concluded that this phenomenon of relief was not disease-specific-but group-specific. Among the substances which they considered in 1938 was listed adrenal cortical extract. Along these lines, therefore, Compound E was first injected into a patient with rheumatoid arthritis on September 21, 1948. The effect of Compound E on rheumatoid arthritis was reported on April 13, 1947 (7), and shortly thereafter, there were rumors of a sharp increase in the sale of Vitamin E. For this reason, it seemed desirable to give Compound E a distinctive name. Hench and Kendall chose the name "Cortisone."

III. CHEMICAL STRUCTURE OF THE CORTICAL STEROIDS AND THE RELATION TO PHYSIOLOGICAL ACTIVITY.

Of the twenty-eight chemically-pure compounds which have been isolated from the adrenal cortex, only six appear to have the physiological activity of the adrenal cortex. Others

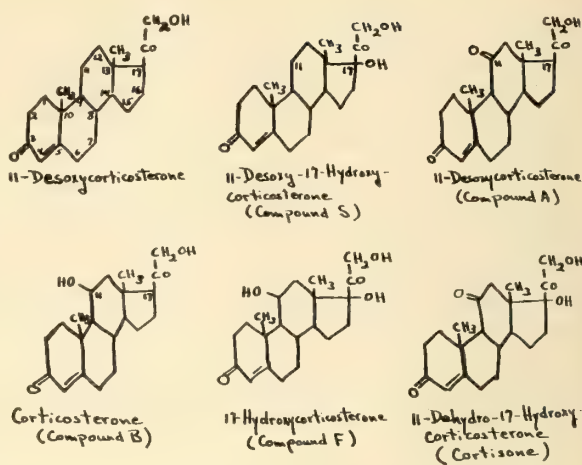


Figure I.—Steroids with known physiologic activity isolated from adrenal cortical tissue.

have sex activity and as for the remainder, the amounts have been too small for clinical investigation. The six adrenal corticoids are illustrated in Figure I. They all possess the following chemical groupings in common:

- A ketogenic oxygen at the C-3 position
- A double bond between C-4 and C-5
- A side chain at C-17 which carries a ketone adjacent to a primary alcohol (the alpha-ketol groupings, as in fructose).

Also, it is to be noted that the two desoxy compounds are characterized by the absence of oxygen substituted in the C-11 position. The remaining four steroids are characterized by the presence of an atom of oxygen, either a ketone or a hydroxyform, at the C-11 position. These compounds are variously called 11-oxysteroids, oxygenated C-11 steroids or sometimes simply corticosterones.

Dehydrocorticosterone, corticosterone, and cortisone were synthesized from desoxycholeic acid, a constituent of bile.

The relationship between physiologic activity and chemical configuration among the adrenal corticoids is indeed very interesting. For example, 11-desoxycorticosterone whose major difference from the Compound F-like steroids is the absence of oxygen at C-11 position, effects electrolyte metabolism mainly. It has no effect on carbohydrate, protein, or fat metabolism. Neither does it effect the cellular elements of the blood or tissues. On the other hand, 11-oxysteroids are chiefly concerned with the metabolism of carbohydrate, protein, and fat. The C-11 oxygenated steroids also exert a definite

effect upon the hematopoietic system and tissue cells.

In respect to physiological activities, what are adrenocorticotrophic hormone, and Cortisone? As most of you know, ACTH is a protein substance of high molecular weight (20,000) produced by the anterior pituitary. Relatively recently, Li (8) has shown that a protein-free peptide mixture prepared from whole adrenocorticotrophic hormone has been found to have a high degree of adrenocorticotrophic activity. The exact size of this peptide is not exactly known, but appears to be in the neighborhood of 1,000. In this range synthesis is not only possible but probable. ACTH has but one function, and that is to stimulate the adrenal cortex to function. When stimulated, the adrenal cortex produces many steroidal hormones, and now we know that they are chiefly Compound F-like steroids with possibly only traces of Cortisone. Chemically, therefore, ACTH and Cortisone are entirely different, and the common denominator in their effectiveness against a wide variety of disease states is the activity of Compound F-like hormones.

IV. THE ALARM REACTION AND GENERAL ADAPTATION SYNDROME

A. *The Alarm Reaction:*

"The alarm reaction", as a clearly defined separate entity, was first described by Selye in 1936 (9), and because of its close association with the role of ACTH and Cortisone it becomes important that an understanding of this phenomenon be obtained.

It was realized that in response to a great variety of toxic agents the organism responds with the same set of symptoms. The reaction consists of two more-or-less distinct phases, and it is initiated by an acute "stress" situation, such as trauma, surgery, infection, etc. . . See Figure II. The first or "shock phase" is characterized by: tachycardia, decrease in muscular tone and body temperature, formation of gastric or duodenal ulcers, hemoconcentration, anuria, edema formation, decrease in blood chlorides, acidosis, and a transitory rise followed by a decrease in blood sugar, leukopenia followed by leukocytosis, and a discharge of adrenalin from the adrenal medulla. It is the stimulation of the anterior pituitary gland to put out ACTH which in turn stimulates the adrenal cortex to secrete its protective corticoids that counterbalances the effect of the "shock phase." This phase may last any-

where from a few minutes to twenty-four hours, and unless the termination is fatal, it is followed by a second or "counter-shock phase." There occurs a reversal of most signs characteristic of the shock phase. Thus, there is blood dilution and increase in blood volume, increase in blood sugar and blood chlorides, alkalosis, diuresis, and often a rise in body temperature.

If the animal is maintained under the stress or "alarming stimulus", as Selye, calls it, that produced the shock phase the counter-shock phase gradually merges into the "stage of resistance", during which most of the morphologic lesions regress and specific resistance reaches its peak.

Finally, it was found that even a perfectly adapted organism cannot indefinitely maintain itself in the stage of resistance. If exposure to abnormal condition continues adaptation wears out; the lesions characteristic of the alarm reaction as involution of the lymphatic structures, adrenal enlargement, gastro-intestinal ulcers reappear and the "stage of exhaustion" develops during which further resistance becomes impossible and death ensues.

B. *General Adaptation Syndrome:*

Selye feels that when the pituitary-adrenal hormonal adaptation mechanism breaks down a variety of diseases may occur. He feels there is enough evidence to show that hypertension, nephrosclerosis and periarteritis are probably due to abnormal adaptive processes. Other diseases are also listed in order to call attention to their possible connection with the general adaptation syndrome. He produced morphologic lesions in the kidneys of experimental animals that were unilaterally nephrectomized and fed high protein and high salt diets which resembled nephrosclerosis; lesions in arteries resembling those of periarteritis nodosa; Aschoff bodies in the myocardium similar to those seen in rheumatic carditis; these changes were not infrequently associated with hypertension and arthritides. These changes were produced by the administration of large doses of pure synthetic desoxycorticosterone acetate as well as anterior pituitary extracts. All experimental observations are most readily compatible with the view that during the general adaptation syndrome, certain hormones of the anterior pituitary and adrenal cortex are produced in excessive amounts in order to increase resistance; this defensive endocrine response is valuable in as much as it

facilitates adaptation to stress (i.e., infections, intoxications, nervous commotions, cold, etc. . .), but the resulting endogenous hormone over-dosage with an imbalance of excess mineralocorticoids over glucocorticoids may become the cause of certain cardiovascular, renal and joint diseases. This, Selye has termed a "derailed" adaptive response. Therefore, administration of cortisone counterbalances the excess desoxycorticosterone-like steroid production resulting in a more normal adaptive response to stress. Thus developed the concept that many of the most common maladies of man are "diseases of adaptation", that is to say, the by-products of abnormal adaptive reactions to stress.

V. METABOLIC AND PHYSIOLOGIC EFFECTS OF ADRENAL CORTICAL STIMULATION

The metabolic and physiologic effects (Figure III) of adrenal cortical stimulation by ACTH suggests that there are possibly three different types of hormones secreted by the adrenal gland: namely,

A. *Desoxycorticosterone-like Hormones:*

This group of hormones causes retention of sodium and chloride with concurrent retention of fluids and decreased sweating. Increased excretion of potassium may result, to some extent from the displacement of intracellular potassium by the retained sodium.

Additional potassium loss may occur in the early phase of ACTH and Cortisone administration. This may be followed by a phase of potassium retention by the liver together with the increased glycogen deposition and finally there is an actual loss of intra-cellular potassium in the course of the establishment of a negative nitrogen balance due to increased protein breakdown. This anti-anabolic effect produced by excessive ACTH stimulation may be obviated in part by the anabolic action of testosterone or adrenal "androgens", and thus correct to some extent the increased excretion of potassium. Increased stimulation of the adrenal cortex by ACTH may produce a hypokalemic, hypochloremic alkalosis such as is seen in Cushing's syndrome from over-excretion of the potassium ion resulting in fatigue and electro-cardiographic changes characteristic of potassium deficiency.

Excessive adrenal cortical activity seems to withdraw calcium and phosphorus from bone into the extracellular fluids from which they are excreted into the urine and feces. This finding

appears to be correlated with a fall in alkaline phosphatase. Decreased osteoid formation with less laying down of bone to explain these shifts has been reported. This may well explain the osteoporosis commonly seen in Cushing's syndrome. However, this has not been seen with doses now employed.

Compensating mechanisms come into play, causing most individuals to diurese retained fluids, sodium and chloride and begin to retain potassium while still on the same dose or when it is decreased. There is some evidence that the adrenal cortex can secrete corticoids that actually cause excretion of sodium and chloride and retention of potassium. This electrolyte effect and resulting edema is not serious if carefully observed for it may correct itself while on the same dose or it can be corrected by lowering the dose, omitting several doses or by putting the patient on a low salt, high potassium intake.

The Compound F-like hormones also have an electrolyte effect similar to the desoxycorticosterone-like hormones. However, the effect is less marked. The desoxycorticoids, on the other hand, have none of the metabolic or physiologic effects characteristic of the Compound F-like hormones.

B. *Compound F-like Hormones, or 17 Hydroxycorticosterone-like Steroids:*

There is evidence that the human adrenal cortex secretes Compound F-like hormones and not Cortisone, which is secreted only in trace amounts, if at all. These hormones affect the intermediary metabolism of carbohydrate, protein, and fat.

1. *Carbohydrate:*

They cause glycconeogenesis or conversion of glucose to glycogen in the liver and muscles to restore the glycogen stores that are used up in the "alarm reaction," or reaction to acute "stress" situations. Over-stimulation of the adrenal cortex may even produce glycosuria with or without hyperglycemia. Glycosuria without hyperglycemia has been interpreted as due to a lowering of the renal threshold. The glycosuria with hyperglycemia may result when utilization of glucose and formation and deposition of glycogen cannot keep pace with the rapid mobilization of sources of energy (as conversion of amino acids and possible fats to glucose) and their conversion to glucose. The hypoglycemia and glycosuria, therefore, are not indicative of a true diabetes, but merely represent too rapid

mobilization of energy sources. However, latent diabetes in those individuals with a family tendency are more prone to develop a diabetes-like state. It has been suggested that ACTH be used as a test to bring out this tendency in these cases when the diagnosis is questionable. This condition is relatively resistant to insulin as is similarly the diabetes seen in Cushing's syndrome. It only occurs on high doses of ACTH or Cortisone and it will disappear when the dose is lowered or the hormones stopped.

During ACTH therapy, fasting blood glutathione decreases as carbohydrate tolerance is lowered (10). Administration of reduced glutathione during a course of ACTH induced diabetes produces temporary cessation of glycosuria and a fall of blood sugar (11). Thus, glutathione antagonizes the diabetogenic effort of ACTH.

2. Protein:

Compound F-like steroids display an anti-anabolic effect by the mobilization of amino-acids from tissue proteins, partly as a source of energy, partly for conversion to glucose and glycogen (carbohydrate-sparing effect), and partly to make amino acids available for protein synthesis in injured or abnormal tissues. The extent to which a negative nitrogen balance is established depends upon the relative increase in the 11-oxysteroids and androgenic steroids under the action of ACTH in any given case. The creatinuria and increased excretion of uric acid would be compatible with this increased catabolism of protein.

3. Fat:

They also mobilize fat from the fat depots as a source of energy and possibly for conversion to glucose and glycogen (carbohydrate-sparing effect). There occurs an increased production and utilization of fat with a decrease in the respiratory quotient and other metabolic pathways of fat. After an initial transitory rise, this is reflected by a lack of ketone bodies in the blood and urine, as well as the absence of acidosis. In summary, the above effects of the excessively stimulated adrenal cortex is reflected in:

- a. Increased excretion of nitrogen;
- b. Increased excretion of potassium;
- c. Increased excretion of phosphate;
- d. Increased excretion of calcium.

Therefore, it becomes apparent that the main metabolic action of this group of the Compound F-like steroids is in the mobilization of

sources of energy and restoring sources of energy in the form of glycogen in the body.

Studies still in progress at the Donner Laboratories with ACTH and Cortisone in atherosclerotic rabbits indicate striking changes in the serum levels of the various giant lipo-protein molecules (cholesterol-containing), which consists of an initial drop followed by a rise (12).

C. Adrenal Corticoandrogens:

Adrenosterone-like steroids are also secreted by the adrenal cortex and appear to have an anabolic function when contrasted with the catabolic effects of compound F-like hormones such as Cortisone. As judged by signs of masculinization in some individuals (especially dark skinned, hairy women), ACTH appears to increase the secretion of adrenosterone-like compounds. Adrenosterone-like corticoids may induce a positive nitrogen balance and increase body protein in contrast to Compound F-like hormones. The ratio of the amount secreted between these two groups of steroids by the adrenal cortex may be a major determining factor in the over-all effect of the adrenal cortical stimulation by ACTH on the total body proteins.

A close functional inter-relationship exists between the adrenal and thyroid glands. For a number of days ACTH may reduce the basal metabolism rate. This may be due to the inhibition of the pituitary thyroid stimulating hormone (TSH) and is reflected in a decreased rate of uptake of radioactive iodine by the thyroid and by a lowered plasma protein-bound iodine concentration—a measure of circulating thyroid hormone.

On the other hand, ACTH seems to exhibit a calorogenic effect through the stimulation of the secretion of Compound F-like steroids. The basal metabolic rate may actually rise. In Cushing's syndrome, the basal metabolic rate is usually low, although it may be either normal or above normal depending on the degree of inhibition of pituitary thyrotropin secretion and the quantity and type of adrenal corticoids being secreted by the adrenal gland.

VI. EFFECTS OF ADRENAL CORTICAL STIMULATION ON BLOOD

A. *Cytology*: The following effects are due to Compound F-like steroids:

1. *Red Cell Series*: These hormones have been shown to induce a marked reticulocytosis in various diseases (even in pernicious anemia). Prolonged ACTH therapy leads to a general

increase in the number of red cells. However, long standing plastic anemia is not effected. The hematocrit is usually lowered in the initial period of ACTH administration because of water retention and hemodilution. However, following reticulocytosis, the hematocrit may show a gradual rise often increased by the gradual decrease in water retention which occurs on prolonged ACTH therapy.

2. *Leukocytic Series:* ACTH and Compound F-like hormones tend to induce a marked leukocytosis and a shift to the left in most instances. Eosinophiles decrease in the circulating blood, the maximal drop occurring some three to four hours after a single injection of ACTH and culminating in their eventual disappearance on continued administration. Bone marrow production remains the same or actually increases. The ultimate fate of eosinophiles is not known, but indirect evidence suggests that they are destroyed at a more rapid rate than normally. It is on this phenomenon that "The Four-Hour ACTH Test", as devised by Thorn (2c) for estimating adrenal cortical functional reserve is based. A percentage fall in eosinophiles of fifty per cent or more below the pre-injection level and an increase of fifty per cent or more in the uric acid creatinine ratio over the pre-injection ratio usually indicates a satisfactory adrenal cortical response. Under the cortical hormones, Compound F-like, lymphocytes are destroyed. Lysis of lymph nodes in man appears to be relatively limited. The platelet count is inclined to rise. Evidence suggests of a possible relation of the destruction of basophiles to a rise in heparin titre on ACTH. Clinically, however, this has not been borne out; conversely, there appears to be an increased incidence of thromboembolic disease.

B. Blood Changes:

1. *Sedimentation rate and plasma fibrinogen.* In diseases reversed by ACTH or Cortisone, and in which these are high, there is a tendency toward a return to normal levels.

2. *Gamma globulin.* Concurrently, or shortly thereafter, there is a trend for this to return to more normal levels under ACTH or Cortisone therapy as in disseminated lupus erythematosus.

3. *Albumin.* In nephrosis and malnutrition, where the serum albumin may be below normal, there is a tendency to return to normal levels on continued ACTH administration.

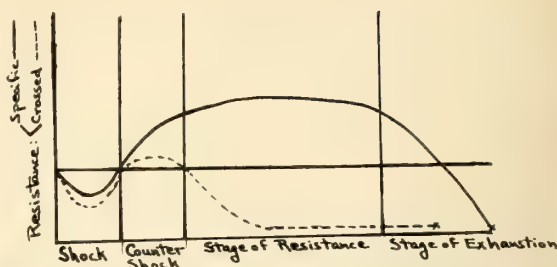


Figure 2.—Alarm Reaction.—Schematic representation of the changes in specific (full line) and crossed (dotted line) resistance during three stages of the General Adaptation Syndrome (Selye).

VII. EFFECT ON ENZYME SYSTEMS

1. *Hyaluronidase:*

Hyaluronidase, or the spread factor, is inhibited in part. This function of ACTH may be an important one by decreasing the shifts of body fluids and materials dissolved in them, and by reducing the intensity of the inflammatory reaction.

2. *Lysozyme:*

It is found in low concentration in the small intestine and in excessive amounts in ulcerative colitis. ACTH greatly decreases the concentration of lysozyme in the latter disease and healing of the ulcerated mucosa proceeds as the intensity of the inflammatory reaction subsides.

3. *Pepsin, Pepsinogen and Urepsin:*

All three show a marked rise during ACTH and Cortisone therapy. Two clinical facts come to mind—the marked rise in appetite found in so many patients, and the deleterious effects in the treatment of gastric ulcers with ACTH in a few human subjects.

4. *Serum Peptidases:*

These rise on ACTH therapy. Since these enzymes enhance the breakdown of protein fragments, their rise may possibly have some significance in connection with the catabolic effect of ACTH and Compound F-like hormones.

5. *Arginases:*

This enzyme is increased on ACTH and may also be related to the anti-anabolic effect of ACTH and cortical steroids.

6. *Histaminases:*

It has been reported that histaminase is increased in both tissue and serum on adrenal cortical stimulation, and this may be one clue to the mechanism of action of the adrenal cortex in hypersensitive states. The characteristic reaction to administered histamine persists unchanged on ACTH. An increased amount of

histidine is found in the urine on ACTH as first reported by Holbrook et al.

Histamine, the biological product of histidine, is formed from it under enzymic or enzymatic action. This is inhibited by Compound F-like hormones (1) and (2). The same hormones also increase urinary excretion of histidine (1) and the destruction of histamine by histaminase (3).

VIII. METABOLIC DEGRADATION PRODUCTS OF ADRENAL CORTICOIDS

- A. 11-Oxysteroids. If an adequate reserve of adrenal function is present, ACTH produces a marked rise in the excretion of 11oxy and 17-hydroxylike corticoids. A majority of this increased excretion is 17-hydroxycorticosterone, or Compound-F.
- B. 17-ketosteroids. A portion of the 17-ketosteroids represents androgenic steroid and breakdown products of some of the Compound F-like steroids, such as Cortisone. In the male the testicular secretion provides one-third of the normal value of 17-ketosteroid excretion, whereas in the female the adrenal accounts for most, if not all, of the 17-ketosteroids found in the

urine. Following the administration of ACTH there is significant rise in the 17-ketosteroid excretion, due in part to increased formation of adrenal androgens, but also in part to the metabolic breakdown products of Compound F-like steroids such as 17-hydroxycorticosterone and Cortisone. These changes in the 17-ketosteroid excretion are thus a good over-all measure of adrenal cortical activity. It is interesting that an actual decrease in the excretion of this type of compound in patients on medium-sized doses of 17-hydroxycorticosterone or Cortisone, may occur, and this reflects a functional adrenal cortical inhibition.

IX. FUNDAMENTAL AND BROAD PHYSIOLOGICAL PHENOMENA OBSERVED ON ADRENAL CORTICAL STIMULATION.

In general and quite apart from all the above phenomena, there are certain basic phenomena that should be considered for they may be related at the very fundamental tissue cell level to disease processes and their reaction to ACTH administration.

A. ACTH Appears to Render Cells Immune

FIGURE III.—Metabolic and Physiologic Effects of Adrenal Cortical Stimulation

Increased Excretion of N	Sed. Rate, Plasmo Fibrinogen,)Toward Gamma Globulin, Albumin)Normal
Increased Excretion of K+ (Electrocardiographic Changes)	Hyaluronidase Inhibited Lysozyme Decreased
Increased Retention of Na+ & CL- (edema)	Pepsin, Pepsinogen, Urepsin Rise Serum Peptidases, Arginase Rise
Increased Excretion of P+ & Ca+	Histaminase Activity Increased
Glycosuria with or without Hyperglycemia	Histamine Decreases, also Histidine Excretion Increases
Anti-insulin Effect	11-Oxysteroids & 17-Ketosteroids Increased in the Urine
(GSH Antagonizes Diabetogenic Glutathione Decreases Effect of ACTH)	Cells Rendered Immune to Toxic Agents (Bacteria, Antigens, Chemicals)
Anti-anabolic Effect (CHO-Sparing Effect)	Inflammatory Reaction Inhibited
Creatinine Excretion Increased	Fibroblastic Proliferation Inhibited
Uric Acid Excretion Increased	Fever and Pain Inhibited
Increased Production, Mobilization and Utilization of Fat	Wound Healing Delayed BP Normal or Increased
BMR Decreased	Euphoria to Psychosis
Giant Lipo-protein Molecules Increased	Androgenic Effects (acne, hirsutism, amenorrhea, thinning of hair)
Reticulocytosis, Leukogtosis (with Shift to Left)	In Males—Importance & Sex Drive
Circulating Eosinophiles Decrease (Thorn Test)	Adrenal Atrophy or Hypertrophy
Lymphocytopenia, Basophilopenia, Platelets Increased	Miscellaneous—Moon Face Buffalo Hump, etc. . . .

to a Wide Variety of Known Toxic Agents. For example:

1. *Bacteria.* A patient may have peritonitis or a pneumococcal septicemia without fever, or any clinical evidence of infection. The pneumonia may resolve rapidly.

2. *Antigens.* Highly sensitive individuals may be exposed to specific antigens or drugs while under ACTH administration with no deleterious effect. This may be related to the possible mechanism involved in effecting a decrease in tissue histamine as just described.

3. *Chemicals.* A patient sensitive to iodine, aminopterin, or mustard gas will show no idiosyncrasies toward these chemicals while on ACTH.

B. Inhibition of the Acute Inflammatory Reaction:

ACTH will inhibit or block acute inflammatory reactions from almost any cause. Thus, the peritoneal cavity may be grossly contaminated by gastric or fecal material, yet there will be little to no inflammatory reaction in the peritoneum. In the near future it will have to be decided just what constitutes a beneficial inflam-

matory response and doses of ACTH and Cortisone will have to be adjusted accordingly for optimum benefit.

C. Inhibition of Excessive or Prolonged Fibroblastic Proliferation:

ACTH inhibits or blocks excess fibroblastic proliferation almost regardless of cause. This may well be one of the basic mechanisms involved in a number of chronic proliferative diseases, such as rheumatoid arthritis.

D. Inhibition of Fever:

Adrenal cortical stimulation appears to inhibit fever from almost any cause.

E. Inhibition of Pain:

Whatever the cause, pain is inhibited or blocked by the administration of ACTH.

A patient on prolonged ACTH administration suddenly developed an unexplained tachycardia for several days, and no other significant signs or symptoms. ACTH was stopped and in a matter of hours he began to complain of substernal pain radiating to the left shoulder, and developed fever, leukocytosis, etc., the typical clinical picture of coronary occlusion.

FIGURE IV

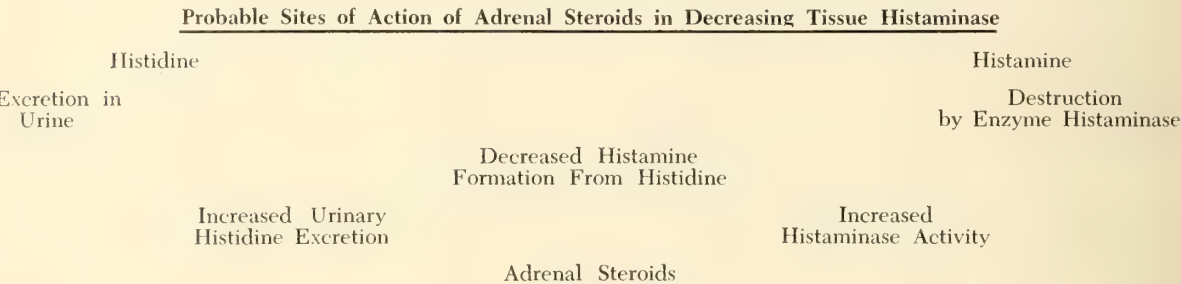


FIGURE V.—The New England Journal List of the Preliminary Grouping of Disease on the Basis of the Response to ACTH and Cortisone Therapy

Diseases in Which Drugs Are Most Useful	Diseases In Which Drugs May Be Useful	Diseases In Which Drugs Are of Questionable Value	Diseases In Which Drugs Are Of No Value	Diseases In Which Drugs May Be Detrimental
Addison's Disease (Cortisone on y)	Rheumatoid Arthritis	Mental Disease	Herpes Simplex	Diabetes Mellitus
Panhypopituitarism	Psoriasis	Multiple Sclerosis	Herpes Zoster and Varicella	Cushing's Syndrome
Functional Adreno-Cortical Insufficiency	Disseminated Lupus	Pemphigus	Scleroderma	Hypertension (ACTH)
Functional Hypopituitarism	Erythematosis	Myasthenia Gravis	Progressive Muscular Dystrophy	Congestive Heart Failure
Anorexia Nervosa	Dermatomyositis	Osteoarthritis	Paget's Disease	Osteoporosis
Idiopathic Hypoglycemia	Periarteritis Nodosa	Tuberculosis	Atrophy	Acne
	Acquired Hemolytic Jaundice	Pneumonia	Cystic Fibrosis of Pancreas	Hirsutism
Acute Rheumatic Fever	Vasomotor Rhinitis	Anoxia	Pernicious Anemia	Peptic Ulcer
Acute Gouty Arthritis	Urticaria	Liver Disease	Thyrototoxicosis	Sarcoidosis
Status Asthmaticus	Multiple Myeloma	Malignant Exophthalmos	Glomerulonephritis	
Serum Sickness	Lymphoma	Cancer	Hypertension (Cortisone)	
Exfoliative Dermatitis	Leukemia			
Loeffer's Syndrome	Nephrotic Syndrome			
Acute Inflammatory Disease of Eye	Ulcerative Colitis			
	Regional Enteritis			
	Pulmonary Berylosis			

F. Adrenal Cortical Stimulation and Central Nervous System Physiology:

Regardless of the disease in question, most patients receiving ACTH are inclined to develop a sense of well-being and a sense of mental activity bordering on euphoria. When relief is obtained from a chronic, painful, debilitating disease, the sense of well-being may be a natural consequence. However, electro-encephalographic recordings on patients on ACTH administration reveal that the alpha waves are of both larger magnitude and shorter intervals, suggesting that there is an effect upon the physiology of the individual neurones. Therefore, the patient on high doses of ACTH should be carefully observed from a psychiatric viewpoint since overstimulation may bring subclinical psychoses to the clinical level in rare cases.

G. Additionals

Two unpleasant complications of prolonged therapy with ACTH or Cortisone have been clinically noticed by local observers which, heretofore, have not been reported in the literature. There is what appears to be an increased incidence of thromboembolic accidents and second the occurrence of pathological fractures from minimal trauma, no doubt a result of the osteoporosis which develops on prolonged administration of these substances.

X. EFFECT ON DISEASES:

Time does not permit a detailed account of the great number of diseases studied which either respond very dramatically or at least show some improvement with either ACTH or Cortisone therapy. I will merely mention certain diseases that have responded exceedingly well, and others that have responded enough to warrant careful continuation of studies. Figure V. shows examples of diseases treated using the New England Journal List as an outline. In addition to rheumatoid arthritis, acute rheumatic fever, chorea, disseminated lupus erythematosus, periarteritis nodosa, dermatomyositis, and scleroderma are included, plus many varied diseases which appear to have no relation, such as ulcerative colitis, malignant exophthalmos, Grave's thyrotoxicosis, spontaneous hypoglycemia, gout, acute nephritis and nephrosis, and malignant lymphomas have been affected importantly, as have various types of leukemia.

Early silicosis and beryllium granulomatosis (13) respond to ACTH. Silicosis, as you know, is a disease in which one sees tremendous fibro-

blastic proliferation as a result of the silica. We do not see the silica in the X-ray, but we see much fibroblastic proliferation. If Cortisone stops fibroblastic proliferation, then we can see some possibility for explaining this result. In myasthenia gravis, interesting things have been observed with ACTH which require much more study. Certain diseases, like primary atypical pneumonia and acute hepatitis, have responded dramatically to these compounds. Findland (14) has found some very important effects in pneumococcal pneumonia, as mentioned earlier.

Recent reports indicate that in exudative pulmonary tuberculosis, the exudation disappears very rapidly. Keep in mind that one must be very careful with respect to tuberculosis, since it must be realized that there is an inhibitory effect upon fibroblasts. These hormones could conceivably prevent or break down a cellular barrier and allow a spread of active tuberculosis.

Iritis, uveitis, interstitial keratitis, and other ophthalmological conditions respond to these materials, where other treatments have failed.

In major surgery, the adrenal hormones of the "11-17-oxy" type are of vital importance in the reaction of the organism against stress. Hence, clinically it would be of great importance to be able to reveal the presence of these hormones in adequate amounts. Thorn (2d) and workers have studied this problem. To test adrenal cortical function, two methods were used as indices, (1) The Four-Hour ACTH Test, and (2) The Epinephrine Test. The administration of ACTH or Epinephrine both lead to an eosinopenia. A fall of 50% or more four hours after the injection of either of these compounds is considered a normal response. The two tests differ in the mechanism of the production of this response; ACTH by directly stimulating the adrenal cortex, and Epinephrine by stimulating the pituitary-adrenal mechanism (or the hypothalamic-pituitary-adrenal mechanism).

In the presence of normal adrenal cortical activity, there is an almost complete disappearance of circulating eosinophiles during the first 24-48 hours after a major operation (counter-shock phase of The Alarm Reaction). This is in itself evidence of increased cortical activity. Conversely, the finding of a normal or high eosinophile level during the first 24-48 hours after an operation suggests adrenal cortical insufficiency, in the absence of allergy. Approximately 72 hours post operatively, there is usually a sharp

rise of the eosinophile level, apparently indicating a return of adrenal cortical activity to a more normal plane. The use of The ACTH Test before surgery is a good index of the capacity of the adrenal cortex to excrete 11-oxysteroids and furnishes a good means of pre-operative prognosis.

It is now apparent that ACTH given intravenously will be a valuable adjunct to the therapy of acute traumatic shock, severe burns, long shocking operations, poor surgical risks, and even in the shock produced by acute blood loss.

XI. SIGNS AND SYMPTOMS OF OVER-STIMULATION

Briefly, let us summarize the clinical evidence of over-stimulation:

1. *Edema.* A rapid, unusual weight gain may be an early indication of impending edema. This can be minimized by a low salt, high potassium intake, decreasing or omitting doses, and diuretics. Recently, certain resins given orally affecting ion transfers in the gastro-intestinal tract are said to aid in the excretion of sodium.

2. *Weight loss or nitrogen loss.* Usually this effect is minimized by a high protein diet or by the administration of 25 mg. of testosterone daily by mouth. Again, recently, an androgen has been found that has the anabolic effects of testosterone but little to none of the masculinizing properties of the latter.

3. *Hyperglycemia and glycosuria.* This is seldom a problem except in those patients with a familial background. Usually it is controlled either by lowering the dose or administering insulin.

4. *Hypertension.* Daily routine blood pressure readings should be done. Hypertension may be transitory during the period of electrolyte and water retention. It may be controlled by decreasing the dose. If it persists ACTH should be discontinued. Persistent hypertension may reflect parenchymatous renal disease, as in some cases of disseminated lupus erythematosus.

5. *Muscle weakness, fatigue, exhaustion or paresthesias.* These may be a reflection of potassium deficiency and blood potassium levels and electrocardiograms should be obtained. In most cases these signs and symptoms, if due to potassium deficiency, can be corrected by increasing the potassium intake and lowering the dose of ACTH. Suppression of the adrenal cortex

after prolonged Cortisone administration has been incriminated.

6. *Disturbed psyche.* The patient should be observed for exaggerated euphoria or nervousness and pronounced insomnia or depression. If these occur ACTH should be reduced and proper sedatives given as indicated. Should psychotic changes become severe or persist, ACTH should be stopped, sedation and possibly other measures instituted as indicated.

7. *Miscellaneous effects.* Rounding of the face (moon-face), the fat pad between the scapulae (buffalo hump), and other distributions of fat peculiar to Cushing's syndrome are seen, even when there has been no significant increase in weight (edema). This has been attributed to redeposition of fat.

Thinning of the skin, reddish or purplish striations, acne, and hirsutism as seen in Cushing's syndrome have been observed both in males and females when ACTH is given in large doses. Amenorrhea may be hormonally induced or maintained. This is more apt to occur in adolescent girls. In males a diminution in sex drive has been observed in some cases. Impotence is a common occurrence in men with Cushing's syndrome.

XII. FUNCTIONAL DEPRESSION OF THE ADRENAL CORTICES

The evidence reported by Sprague (15) and co-workers is strongly suggestive of depression of some functions of the adrenal cortex by Cortisone. After withdrawal of Cortisone, asthenia and impairment of the eosinophilic response to ACTH occur. Also, the urinary excretion of 17-ketosteroids is decreased during administration and after withdrawal of Cortisone. From a practical standpoint, a patient who had recently received Cortisone, the possibility should be borne in mind that the function of the adrenal cortex may be so depressed that it may be inadequate under conditions of stress, such as trauma, infection, etc. The adrenal cortex may be refractory to the administration of ACTH for a variable period after withdrawal of Cortisone.

XIII. DOSAGE AND METHODS OF ADMINISTRATION

In view of the fact that adrenal cortical stimulation affects so many important metabolic and physiologic processes in the body, it is essential to become fully familiar with the changes that may occur on adrenal cortical stimulation with ACTH. Likewise, dosage schedule should

be considered in the light of the alterations that may occur.

Since the adrenal glands of different individuals vary considerably in their sensitivity to stimulation by ACTH, there is no constant, specific, uniform dose that is effective in all individuals. A few individuals need as little as 5 mgm. of ACTH four times a day, while others require as much as 50 mgm. four times a day. This relative effectiveness of ACTH which is also true for Cortisone, may be related to the functional state of the adrenal cortex at that moment. In complete adrenal insufficiency ACTH will produce no effects, whereas, in a functionally large and sensitive adrenal cortex a given dose of ACTH will produce a maximal effect. Cortisone, on the other hand, by inhibiting both endogenous ACTH and the adrenal cortex directly to some extent, will lose a large portion of its potential effectiveness.

In general, however, 25 mgm. of ACTH four times a day is sufficient to cause definite metabolic alterations, therefore, unless a clinical effect is not obtained smaller doses should be used which cause relatively slight or even non-detectable metabolic changes and are still therapeutically effective in a substantial number of various disease syndromes.

It is desirable to start the patient on a 10 to 12.5 mgm. of ACTH four times a day and to hold the patient on this dose level for several days to ascertain if a clinical effect can be obtained. If not, the dose is gradually increased, observing the patient for several days on each dose increment until a clinical effect is obtained keeping in mind the metabolic alterations to be avoided. Each dose is given at six hour intervals in view of the evidence that has accumulated that the clinical and physiological effect of ACTH is largely worn off in this period of time. For prolonged therapy it is desirable to maintain the patient on the smallest clinically effective dose. The administration of ACTH should never be stopped suddenly at a high dosage level, because there is definite evidence that there is a period of adrenal cortical hypofunction (exogenous ACTH may depress production of endogenous ACTH through the increased titre of the adrenal steroids) anywhere from two to five days after cessation of therapy. Tapering off the dose gradually will allow the patient's own pituitary to take over the secretion of en-

dogenous ACTH for his own adrenal cortical stimulation.

Unresponsiveness to ACTH may be due to two general causes: to a relatively poor adrenal cortical reserve, or to a possible occurrence of antibodies against an ACTH preparation. The latter cause is rare and should be thought of when a second course of therapy is begun and a therapeutic effect is not obtained. In such cases ACTH prepared from another species should be used.

As you know, ACTH is a protein substance, and as such it cannot be given orally because of the destructive action of the gastro-intestinal enzymes. It has been prepared in three forms for parenteral use. The preparation now in common use is a dry powder which is extracted from the pituitary glands of domestic food animals and is put in solution by dissolving it in sterile saline. This form is administered intramuscularly and, as already mentioned, its effect is over within six hours. The main objection to this preparation is the necessity of the frequent daily injections. Two longer acting preparations are still in the investigative stage. One is ACTH in propylene glycol which can be given subcutaneously in a single daily dose. Even longer intervals may be effective. The other is ACTH in an oily vehicle, which is injected intramuscularly.

Because of the possibility that some of the ACTH injected intramuscularly may be destroyed by the peptidases in muscle, it may be that the subcutaneous route will be the most desirable although somewhat more painful. The aqueous preparation has recently found a new use in surgery. Small doses of 10 to 25 mgm. may be given intravenously over a period of hours in an infusion to patients preoperatively, during the operation, and post-operatively as the indication arises. Surgical procedures are tolerated extraordinarily well and operations that would otherwise not be attempted can be performed.

Cortisone, on the other hand, is prepared for intramuscular injection as a suspension in saline solution. It is being synthesized from bile acids. As with ACTH, the object of treatment is to obtain the maximum effect with the minimum dosage. The recommended dosage for the initial period in rheumatoid arthritis is as follows:

100 mgm. every 8 hours for 3 doses, then
100 mgm. every 12 hours for 2 doses, then

100 mgm. every 24 hours for 7 to 14 days or less.

When the desired response appears, the dosage is lowered by 10 to 15 mgm. at two to three day intervals until the total daily dose is 50 mgm. This may be changed to 100 mgm. every other day. If any significant relapse occurs, revert immediately to the 100 mgm per day dose until the desired response again appears before lowering the dosage. Dosages in other diseases appear to be comparable to that outlined for rheumatoid arthritis.

Cortisone may be administered orally. However, because of the rapid absorption from the gastro-intestinal tract, the total daily dose is given in equally divided doses every six hours. The maximum clinical and physiological effect of Cortisone by this route appears to reach its peak in three to four hours and is almost completely dissipated in six hours.

XIV. THEORIES CONCERNING THE MACHANISMS OF ACTION.

What is the endogenous mechanism that fires off the pituitary gland to secrete ACTH in response to a stress situation? The most attractive theory to date is that formulated on the basis of Harris's (16) work on the rabbit and Hume's (17) work on the dog (See Figure VI). The phenomenon of activating the pituitary through a peripheral sensory stimulus has been well recognized in relation to the production of gonadotropic hormones. By stimulating the cervix in rabbits, Harris was able to induce pseudo-pregnancy and in the case of ovulation, it is known that rabbits will ovulate only after copulation. As an extension of this prior knowledge, Hume has shown that:

1. Following stress, an intact hypothalamus is necessary for the increased release of ACTH;
2. This hypothalamic control of the pituitary seems to be on a hormonal basis, and
3. Following operative trauma, the release by the pituitary of an increased amount of ACTH is dependent upon an intact nervous connection between the injured area and the brain (even in the completely sympathectomized animal). An interesting point that confirms this is the somewhat delayed eosinophilic response, with respect to speed, in the patient with spinal anesthesia over the patient with general anesthesia. This suggests that the normal adrenal cortical stimulation may not occur until the spinal anesthesia wears off. Preliminary

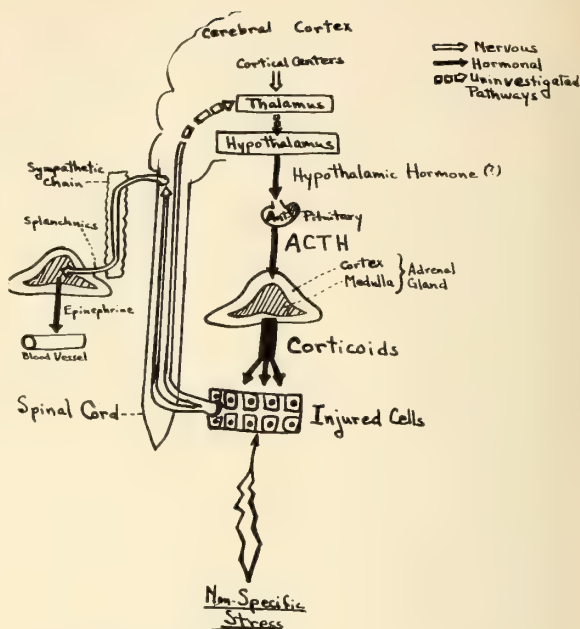


Figure VI: Diagrammatic Representation of the Pathways Involved in the Increased Secretion of ACTH by the Anterior Pituitary Gland.

work with beef hypothalamic extracts seems to indicate that some specific substance is formed in the hypothalamus which will stimulate the production of ACTH from the anterior pituitary gland.

This mechanism of ACTH production may be supplemented by other pathways. For example, a reduction of arterial oxygen saturation to 70-75% was followed by a fall in the circulating eosinophiles of about 40%. This stress may not involve an increased production of adrenalin or the hypothalamic centers, so that it might bring on the secretion of ACTH through increased peripheral utilization of the adrenal cortical hormones.

Toxic metabolic products produced by injured tissues have also been suspected of possibly exerting an effect on the anterior pituitary gland to increase the secretion of ACTH.

The ultimate goal of clinical research is to discover the basic processes that occur at the "tissue level." Are these processes of an enzymatic nature? Is there a decrease in cell permeability since they do not react to known toxic agents? The truth of the matter is that no one knows for sure.

XV. SUMMARY

In summary, suffice it to say that a new era has been opened up which will require a tremendous amount of imagination and work to

arrive at the final answers concerning the true etiology and therapeutics of a large number of diseases that afflict the human race.

I would like to extend my thanks to Dr. C. A. L. Stephens, Jr., and W. Kirby West for their valuable assistance in the preparation of this paper.

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PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL HOSPITAL CASE NO. 28422

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A thirty-four-year-old woman was referred to the hospital because of chest pain.

The patient had been in good health and had been active until about one month prior to admission, when she developed an upper respiratory infection with coryza, slight transient sore throat and malaise. Two or three days afterward, late one afternoon, she suddenly experienced a severe sharp, steady, nonradiating pain in the anterior chest just to the right of the sternum at the level of the fourth rib. The pain was aggravated by coughing and respirations, by lying down on the right side and by downward traction on the right arm. The pain persisted, with sharp exacerbations on coughing, for one week, during which time the patient remained in bed. She was afebrile and there were no sputum, night sweats, hemoptysis, dyspnea, palpitation and orthopnea at that time. On the third day after the onset, her physician made a diagnosis of pleurisy and accordingly strapped the chest, with some relief. Soon after this, she resumed ambulatory activities, but had several more attacks of the same pain, milder in degree and lasting approximately one hour. Because of the persistent pain, an x-ray film of the chest was taken two weeks before entry. This showed "congestion of the right lung." Since the x-ray study, the patient had had no further pain or other symptoms. She had taken no cognizance of her weight variations, but her clothes remained well fitted.

The family history and past history were non-contributory, except that she had occasionally noted ankle swelling in the evening.

Physical examination revealed a well-developed and well-nourished woman in no acute distress. Examination of the heart and lungs was negative. There was slight tenderness on pressure over the spine at the level of the sixth

dorsal vertebra. The abdominal examination was not remarkable.

The blood pressure was 130 systolic, 80 diastolic. The temperature was 99.8°F., the pulse 80, and the respirations 20.

The examination of the blood revealed a red-cell count of 4,770,000 with a hemoglobin of 90 per cent, and a white-cell count of 10,100 with 74 per cent polymorphonuclears. The urine examination was negative, as was the blood Hinton test.

An x-ray film of the chest demonstrated an 8 x 5 x 6.5 cm. slightly lobulated, homogeneous mass in the right cardiophrenic angle. Its anterior surface touched the anterior chest wall, and its lower pole reached to the diaphragm. No calcium was seen within it. The heart and lungs were not remarkable. The diaphragm was normal in position. An x-ray film of the dorsal spine showed no evidence of disease.

Fluoroscopy confirmed the findings of a lobulated tumor in the anterior mediastinum. The fifth day after admission, the patient was operated on.

HOWELL RANDOLPH, M.D.

This protocol contains several rather glaring inconsistencies at which, as practical clinicians, we have learned to look askance. For example there is a careful description of a pain at the level of the right fourth rib, also of a pain at the sixth cervical spine. There is no sputum, but the pain is "aggravated by coughing"; there has been "swelling of the ankles" but they found the cardio-renal system negative in a young woman without cardiac history or other findings to explain it. These statements must be attributed either to an over-zealous resident or to a neurotic patient.

What about the acute respiratory infection at onset? Did that have anything to do with the pulmonary pathology? I don't believe it likely. That infection merely served to call attention to the chest where it settled in that right lung field and was found on the first x-ray. Did the acute shadow obscure the rounded shadow on that first film, or did the "lobulated homogeneous mass" develop following this acute infection? Suppose we follow the latter possibility first. We come up with localized empyema, localized abscess or fungus disease, cystic structures such as echinococcus cyst, torula, hardly tuberculoma in such a short time; but any of these conditions could have been dormant and reac-

tivated by the acute infection.

The "phantom tumor" of the chest is an intriguing condition which may be present one day, disappear three or four days later, and then reappear. Its frequency may be greater than we realize in view of the fact that these patients have not had the frequent routine fluoroscopic observation and chest x-ray that would be needed for its detection. The shadows may be easily confused with those of malignancy or other conditions, but are interlobar in distribution. This condition is the result of cardiac decompensation, and the shadow is produced by a localized pleural effusion. Mercuhydrin produces a dramatic disappearance of the lesion, and the bringing about of cardiac compensation may cure it permanently.

In the case under discussion the final description of the mass on the admission X-ray seems now quite different than on the previous film. A definite circumscribed shadow is described, with the homogeneous character of a solid or fluid consistency. It is spoken of as lobulated, and by this I suppose is meant also that its outlines are well and sharply delineated. There seem to be relatively few things that fit this picture. Pulmonary cysts of long standing which become infected may cause temporary increase in symptoms, with pleurisy and pain fitting this patient's symptoms and this X-ray picture. These cysts are endothelial lined or they may have evolved from respiratory epithelial lined spaces. They may exist within the lung parenchyma, most frequently in the anterior parahilar position, in the dormant state for years. They may have been started by an original infection followed by blocking of the drainage, with a later sterilization of the cavity through natural immunity processes.

The pericardial celomic cyst has a rather similar origin and evolution. Its origin adjacent to the pericardium gives it the name, but it also may be from lung structures. Cystic developments from the esophagus may present in the right side at this low level. The tumor may contain a light brownish material from which colon bacilli may be cultured. Its X-ray appearance is as a large, round circular tumor. It is more posterior than the tumor of our patient.

The paraffinoma is a tumor found in any part of the lung, even the upper lobes, surprisingly enough. It more frequently produces diffuse pneumonitis shadows, but there may be a cir-

cumscribed, rounded and nodular lesion, and this patient's signs could be well explained by such a lesion. The history of mineral oil inhalation has been withheld, however.

Many other lesions of chronic nature might be mentioned such as neurofibroma, hamartoma, bronchial adenoma and arteriovenous aneurysm. A most common lesion is the dermoid cyst, and this location is perhaps the most frequent site of this tumor. On the basis of the most common and likely lesion in this location, my diagnosis is pleuro pericardial cyst, either endothelial lined or with respiratory epithelial lining. Second Diagnosis, Dermoid.

DIFFERENTIAL DIAGNOSIS

Dr. Jacob Lerman: Perhaps we had better look at the x-ray films first.

Dr. George W. Holmes: The shadow that you see in the left lung is not important. Here is the shadow under consideration. Two oblique and a lateral view were taken. I should place the lesion in the anterior mediastinum. The shadow is quite homogeneous, sharply defined and lobulated. That is, it appears to be a solid tumor. So far as we can tell, it is in contact with the anterior chest wall.

Dr. Lerman: Could it be encapsulated fluid?

Dr. Holmes: No, because of the location. We practically never see fluid in that area. The heart and lungs are apparently normal.

Dr. Lerman: The differential diagnosis here centers about the types of mediastinal tumors. I shall first discuss lesions arising outside the mediastinum that eventually lodge in the mediastinum, and second, lesions arising in the mediastinum itself.

One should consider diaphragmatic hernia. Only a very unusual one lodges in the right chest. One might suppose that the hernia went through the anterior attachment of the diaphragm. This type, however, is extremely rare, and I mention it only in passing.

Intrathoracic goiter has to be considered, but it must be of an extremely unusual type to fit this case. Intrathoracic goiters in this region are rare; most occur in the upper mediastinum. Certainly the shape of this tumor is unusual for intrathoracic goiter. Usually, it is a single round nodule and not a lobulated mass that plunges down into the chest to rest on the diaphragm, and it lodges posteriorly rather than anteriorly.

I do not believe this is an aneurysm, because

no definite connection between the mass and the aorta was visualized. The presence of pulsations is not mentioned, although they are not absolutely necessary for diagnosis. Moreover, there is no history or physical findings of syphilis, and the Hinton test was negative. I am not at all concerned about aneurysm.

In considering the diagnosis of mediastinal tumor, one must first settle the question whether the mass is benign or malignant. I think we can state definitely that this mass is not a malignant tumor. The patient was symptomless, except for inconstant pain; there was no evidence of invasion of surrounding structures and organs, and there was no toxemia. Consequently, we can rule out a malignant type of tumor.

Although I doubt that I can make a better diagnosis than just benign mediastinal tumor, I must consider the several varieties. The description of the tumor, the short duration of pain and the unknown duration of the tumor are consistent with dermoid, which also is the most common statistically. On the other hand, several cases with similar findings that have been discussed at these meetings were found to have had either a neurofibroma, chondroma, lipoma or cyst. We saw one mediastinal tumor here a year ago that gave similar symptoms and had a similar appearance in the x-ray films, which the pathologist called hemangioma. One should mention thymoma as a possibility. It must have extended from its origin in the thymus down to this region. I have no way of confirming this diagnosis.

As Dr. Holmes said, it is unusual to find encapsulated fluid in this location, although the history of pleurisy a month before admission raises the question of fluid in the pleural space. Moreover, lobulation of the mass argues strongly against encapsulated fluid. Consequently, I shall not consider it further.

In conclusion, I believe this is a benign mediastinal tumor, either neurofibroma or dermoid.

Dr. William B. Breed: I wonder if enough stress has been laid on the fact that this whole episode was ushered in by an acute respiratory infection. That may be of some importance, and the mass may still be encapsulated pus. Perhaps this point should be stressed just a little more than it was in the discussion.

Dr. Lerman: Dr. Churchill has emphasized many times that the symptoms of these patients

have been influenced by his opinion. Many patients come in with bizarre complaints, and a tumor is found incidentally. I think the onset of the respiratory infection served to focus attention on something in the chest.

Dr. Ralph Adams: Did this mass move with swallowing?

Dr. Tracy B. Mallory: I do not believe so.

Dr. Edward D. Churchill: This is all a guessing game, for it is very difficult to arrive at any preoperative diagnosis except mediastinal tumor, benign or malignant. There are two or three additional diagnoses that occurred to me as I listened to the discussion. I should think of a hernia through one of the apertures of the diaphragm and should have advised a barium enema. There is another lesion that we have come to recognize particularly along the right border of the pericardium,—namely, a thin-walled cyst containing clear fluid. These cysts are comparable to the cystic hygromas that are found in the neck. Perhaps Dr. Mallory can say whether they are of lymphatic origin or of endothelial origin from adjacent serous cavities.

I wish Dr. Holmes would take a stand on the question whether this particular patient should have received a diagnostic dosage of radiation therapy to rule out lymphoma or another radiosensitive tumor before operation.

Dr. Holmes: As a general rule, I think the diagnosis should be established, whenever possible, before we subject a patient to x-ray therapy. But it depends largely on the severity of the operative procedure planned. If it is to be a simple operation, probably x-ray therapy should not be given; on the other hand, if it is a dangerous operation, I should advise giving a small dose.

Dr. Churchill: Will you feel badly if some day I enucleate such a tumor and it turns out to be lymphosarcoma or lymphoma?

Dr. Holmes: No.

Dr. Churchill: Will you, Dr. Mallory?

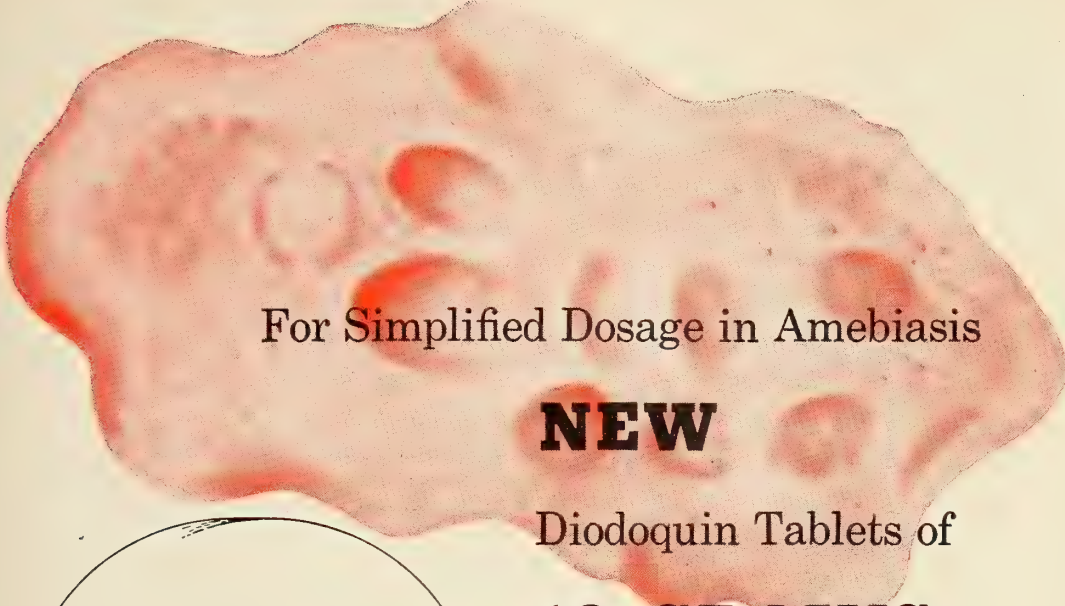
Dr. Mallory: No. It might be good treatment. I think when an isolated tumor is resectable it is wise to remove it, because very long cures often follow the procedure.

CLINICAL DIAGNOSIS

Mediastinal tumor (? dermoid cyst, ? neurofibroma, ? lymphoblastoma).

DR. LERMAN'S DIAGNOSIS

Benign mediastinal tumor (neurofibroma or dermoid).



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SEARLE RESEARCH IN THE SERVICE OF MEDICINE

ANATOMICAL DIAGNOSIS

Pleuropericardial cyst.

PATHOLOGICAL DISCUSSION

Dr. Mallory: This patient did turn out to have a cyst filled with perfectly clear fluid. The cyst has a fibrous wall with an occasional smooth muscle fiber in it, looking essentially like pleura. It is lined with a low cuboidal epithelium that occasionally seems multilayered, which is probably due to tangential sectioning; it seems likely that the epithelium lining was only a single layer thick. So far as the appearance of the cells is concerned, they could either be mesothelial, such as those that line the pleura, or endothelial, which one would find lining a lymphatic vessel. I do not believe I can answer Dr. Churchill's question. I have a little preference for the theory that this sac is made up of pleural or pericardial tissue than that it represents a cystic lymphangiomatous tumor, such as a cystic hygroma of the neck.

Dr. Holmes: Perhaps we should have observed it on inspiration and expiration to see if there was a change in shape, which one might expect if it had a thin wall and contained fluid.

Dr. Mallory: Should this tumor perhaps have been needled before operation?

Dr. Churchill: I do not think so.

Dr. Mallory: If it had been, could you have made the diagnosis?

Dr. Churchill: Probably, but we should not have known what to do in the way of treatment. I do not believe it is without danger to put a needle in so close to the pericardium. There is always a possibility that one is dealing with an aneurysm of the auricle.

Dermoids are likely to be a bit higher on the right and a little closer to the lung root. When a tumor lies in the cardiophrenic angle, a simple cyst must be seriously considered.

Dr. Mallory: Sometimes, there is a rather unusually large amount of fat tissue in that location. Does that ever cause clinical confusion in case of this sort?

Dr. Churchill: I do not recall having been misled by a fat pad.

Dr. Allen G. Brailey: The patient would have been perfectly well if left alone?

Dr. Churchill: I think she would have.

Dr. Mallory: We have no idea of the rate with which these cysts grow. It is quite doubtful that this had anything to do with the symptoms.

Dr. Churchill: I also think that it is very doubtful. One must remember, however, that the presence of an x-ray shadow of this type is sufficient reason for employment rejection by many large industrial plants and, of course, by the armed forces. She can now join the WAACs or WAVES.

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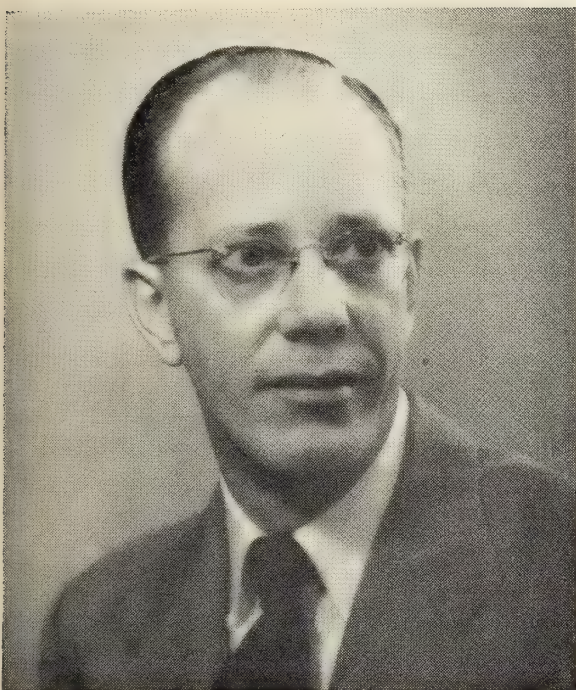
The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

Editorial



L. DONALD LAU
"MR. BLUE CROSS"

In recent years our attention has been directed to such national figures as Bing Crosby, referred to as "Mr. Music"; Joe DiMaggio as "Mr. Baseball"; Senator Robert Taft as "Mr. Republican"; and our own Jacque Mercer as "Miss America."

Within our great state there are also a number of Arizonans, both native and adopted, who have equally distinguished themselves by their singular accomplishments. These talented people, too, have justly earned for themselves the similar titles of "Mr. Music" (Robert Lawrence); "Mr. Baseball" (Del Webb); "Mr. Republican" (Governor Howard Pyle), to mention but a few. Your Editor wishes to add another name to this list—a person whose outstanding accomplishments in his chosen field have rightfully earned for him the title of "Mr. Blue Cross."

As executive director of Arizona Blue Cross-Blue Shield, L. Donald Lau has contributed much in six short years to the economics of the medical profession, the financial stability of our hospitals and the health care of our communities throughout Arizona. Today, Blue Cross' membership consisting of one out of every six and Blue Shield's, one out of every nine per-

sons presently living in the State, stands as mute but effective testimony of the sound, progressive administration and the far-reaching influence of our own hospital and doctors' voluntary, prepayment hospitalization and surgical care plans. Assuming the guardianship of these "adopted children" has been no picnic for Don Lau.

Let's go back a bit.

In 1939, a period when Arizonans were still feeling the depression, William J. Wasson, a present Blue Cross Board member and an active, civic-minded Phoenician, realizing the people, as well as the hospitals of this State were in need of a plan whereby hospital bills could be met through reasonable prepayment methods, conceived the idea (and subsequently was one of its incorporators) of organizing the Associated Hospital Service of Arizona. This Association was patterned after but not approved as a member of the national Blue Cross plans. Operating in a "borrowed" corner of Wasson's office, it started with three hospitals and a limited Service Contract of Benefits. Mr. Wasson also contributed much of his time and effort to organizing and directing the new enterprise. The plan grew, but soon the rumblings of World War II were heard and as a consequence, the plan was put in "moth balls" for the duration.

In the latter part of August 1944, Don Lau had occasion to visit the Valley of the Sun, and like many others before and after him, decided to stay. By mere coincidence he learned of the then dormant Hospital Service Association and promptly made contact. Conferences followed, resulting in Don's being offered the position as director of the plan. Before accepting however, he first decided to make a survey of the leading industries and business firms throughout the State to ascertain whether a Blue Cross plan would receive as favorable reception here as he had, through experience, observed in his native State of Pennsylvania. On his tour throughout Arizona, Don acquired sufficient evidence of interest to write C. Rufus Rorem, then director of the Blue Cross Commission, stating that he would accept the position as executive director of the Associated Hospital Service of Arizona on condition that Blue Cross approval would be secured.

William S. McNary, then executive director of the Colorado Blue Cross plan and also a Commissioner, came to Phoenix on September 11,

1944, to assist L.D.L. in the reorganization process, necessary for eligibility for Blue Cross approval. Conferences with hospital administrators, medical doctors and laymen followed and much midnight oil was spent on the development of new contract benefits, rate structures, corporate policy changes, etc., to meet approval standards. During this time, the two men would meet at their spacious but rather public headquarters—a bench under a certain palm tree in Encanto Park. Finally the mold was complete and McNary submitted his report to the Commission. On October 5th, just six weeks from the time L. Donald Lau took over, the Association received official notification by the Blue Cross Commission in Chicago that it was formally approved as a Blue Cross Plan.

Again, the first official Blue Cross office was a borrowed space in Wasson's office, consisting of two borrowed desks, one borrowed typewriter, a borrowed waste-paper basket, telephone stand one old but usable file. Group enrollment was opened to the public on November 15, 1944 and a little over 200 of the old association memberships were converted to the new Blue Cross contract. The staff consisted of L.D.L. and Miss Alice Murphy. Together, they functioned as the enrollment, service, case, accounting, research, purchasing, personnel, public relations and administration departments all in one. By December 1945, eight more Arizona hospitals received Blue Cross approval, in addition to the three original ones. Over 19,000 people were enrolled through groups and more than \$43,000.00 had already been paid out in hospital bills for the care of its members. The plan's income that year was \$83,610.94. During this period of early growth however, Don was confronted with another major problem, which, if not resolved, would perhaps scuttle all of his previous efforts and the progress thus far attained.

About the end of 1944, Arizona Blue Cross had received notification from the Attorney General's office, by way of a written opinion, that the original Arizona Hospital license to operate, having been granted under the Arizona non-profit law, was, in his opinion, inadequate and that the present Blue Cross Plan was not properly licensed under this law. This, of course, put the new plan in a precarious position legally. Once again, the glow of midnight oil could be seen in the Blue Cross office and

a solution was compounded. In early 1945 the Arizona Medical Association, with the support of the Blue Cross member hospitals and the Arizona Blue Cross Plan, sponsored a special Enabling Act in the special session of the 17th Legislature then convening. Although there were times during these legislative sessions that success appeared doubtful, the Act was passed and became law under Gov. Sidney Osborn's signature on October 3, 1945. Licensure under the new law assured the Blue Cross Plan of a firm legal foundation.

Having weathered this storm, L. Donald Lau went back to the business at hand. Under his watchful eye, Arizona Blue Cross grew in stature and reputation. By 1946, the plan had increased its membership to over 37,000 and had paid out in excess of \$124,000.00 for the year in hospital bills for members' care. Many satisfactory comments were being heralded from all quarters. The doctors were content, the hospitals, through Blue Cross payments, were meeting their financial obligations and the people of Arizona had, for themselves, a satisfactory, workable prepayment health care plan to meet unexpected hospital bills. But it wasn't enough. The population of Arizona, particularly Phoenix and Tucson, meanwhile having increased tremendously and destined to become a "new home" for hundreds of thousands more to come. it was necessary that a more comprehensive program be considered to meet the public need. Blue Cross was entirely adequate for hospital care. What the public wanted was a similar arrangement to help pay for unexpected surgical bills.

As a result, Arizona Blue Shield was born and sponsored by the Arizona Medical Association. In their meeting of June 22, 1946, it was moved, seconded and duly voted that the Association, acting through its House of Delegates, form a corporation under the new Arizona Non-profit Hospital and Medical Service law, for the purpose of establishing a medical service plan for the State of Arizona, to be administered jointly with the Blue Cross Plan and under the direction of L. Donald Lau as executive director for both plans.

Once more, Lau was destined to hit stormy seas, this time of cyclonic proportions. Many of the medical doctors, having returned to private practice from active service, were uninformed of the latest change in medical economics and lacking the knowledge, understanding the

proper viewpoint of a physician's participation in a plan such as Blue Shield, protested vigorously and vociferously. Armed with patience and perseverance, plus a thorough, convincing knowledge of the advantages and benefits derived from this nationally proven method by both patient and doctor, Don Lau gradually overcame the antagonism shown the Arizona Blue Shield Plan. When the storm subsided and Blue Shield enrollment was opened to the public in November 1947, 53% of the licensed doctors of medicine in Arizona had signed participation contracts. In order to receive Blue Shield Commission approval, it was necessary that 50% of the medical doctors participate in the plan. The figure was close.

Today, over 95% of our Arizona Medical Association members are Blue Shield Participating Physicians. Membership in the plan, as of March 31, 1951, stood at 72,879. In a matter of three short years, Blue Shield has paid \$991,428.27 to its doctors for members' care—\$493,981.78 of this amount was paid in 1950 alone, representing a return of 90.4 cents out of every dollar paid into the plan for the year.

In turn, Arizona Blue Cross has become a million-dollar enterprise. Out of \$1,308,504.54 income for 1950, \$1,053,346.15 was paid to hospitals last year for members' care—or a return of 83.7 cents out of every dollar paid into the plan. As of March 31, 1951, Blue Cross has paid \$3,476,057.80 to hospitals since its inception in 1944. Enrollment figures as of the same date show 122,589 members—and both plans are continuing to grow. The present Blue Cross-Blue Shield offices, as compared with their humble beginnings, now consumes the entire second floor of the Arizona Title Building. The

present staff consists of 55 capable employees.

At a meeting of the Blue Cross District Nine Policy-Making Body, held in Little Rock, Arkansas in February 1951, Lau was elected General Chairman of the District, a responsibility requiring his direction of the district's over-all program for the coming year. (Blue Cross District Nine consists of the 10 plans in the Southwestern States of Kansas, New Mexico, Texas, Oklahoma, Missouri, Colorado, Wyoming, Arkansas and Arizona.) He has also been chosen Blue Cross alternate delegate to the American Hospital Association.

The most recent accomplishment of Arizona Blue Cross-Blue Shield has been the winning of national honors for outstanding achievement in public relations during the past year. The "Oscar" was presented to the Plan at the National Blue Cross-Blue Shield Enrollment and Public Relations Conference, held in Chicago last month (July).

Tirelessly, and with little thought of his personal comforts, Don Lau has carefully nurtured these "adopted children" through juvenescence into a healthy maturity, taking their rightful place as full grown members of the health care trial—the Medical Profession—the Hospitals—and Blue Cross-Blue Shield, a powerful public influence nationally and our strongest supporting force to keep medicine free from political contamination.

The task has been great—the accomplishments, many. We have chosen our guardian well.

Perhaps the very title of this editorial, although descriptive and befitting to the individual, may not be, on second thought, sufficiently adequate—a better one might conceivably be "Mr. Accomplishment."

TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER

WHAT SHOULD A DOCTOR DO about Medicine during his vacation? . . . Forget it? Avoid it? Ignore it? . . . Should he study it, review his plans, see other methods of practice? . . . Should he keep in touch with certain patients? Is he indispensable to some? Will a few wander away? Should he care? . . . Should he spend time on physical exercise? Get more rest? Try a change? Travel? Be with the family? . . . Tough

problem. Should I be wondering about it on a vacation?!

The IMPROVEMENTS IN PENICILLIN are now being more certainly defined. They hugely reduce the allergic effect—a complication which follows in 6 to 10 per cent of the ordinary usage. . . . Several workers have described preparations which seem to be hypo-allergenic, and also desen-

sitizing. . . . One is a biosynthetic analogue (cousin) and the others are salt (relatives by marriage). . . . They are therapeutically equal to the standard penicillins.

The NAMES which are given to most of the TRADE-PREPARED DRUGS are quite mystifying. One wonders why they were chosen—and also what they mean. . . . It must be hard eternally to be original and simple and graphic in such a crowded field. An example of success could be 'Sulfabiotic'; it is a combination of sulfonamides and penicillin, and one can guess it from the name. . . . On the other hand we have 'Pabalate', 'Priscoline', and 'Tromexan'. 'Pabalate' could mean a new form of baby food, but it is a combination of para-aminobenzoic acid and sodium salicylate. 'Priscoline' doesn't suggest the drug (benzazoline) or its use as a vasodilator. 'Tromexan' sounds like a foot-powder from below the Rio Grande—instead of an anticoagulant. . . . What those companies need is someone who can make puns.

The report of Russek and colleagues in a recent JAMA should help resolve the ANTICOAGULANT-MYOCARDIAL INFARCTION problem, since most of us hate to use a hazardous drug in the absence of laboratory controls. . . . They divided their intreated cases according to the presence or absence of CRITERIA WHICH WOULD GIVE A GUARDED PROGNOSIS.—1. previous infarction; 2. intractable pain; 3. extreme or persisting shock; 4. notable cardiac enlargement; 5. gallop rhythm; 6. congestive failure; 7. auricular fibrillation or flutter, ventricular tachycardia, and intraventricular block; 8. diabetic acidosis or other serious disease. . . . More than 200 patients had NONE of the reasons for guarded prognosis; the mortality was 2.45 per cent, and the incidence of thromboembolic disorders was less than 1 per cent. More than 200 other patients had ONE OR MORE signs of unfavorable prognosis; 44.5 per cent died, and 7.7 per cent had thromboembolism. . . . The conclusions suggest that Dicumarol need only be used in those cases in which the signs and symptoms suggest a poor prognosis without it.

The DRUG-HOUSES have been given quite a few laurel wreaths in this column. Many of them rightly should stand high with the profession and the purchasing public. . . . Now we find an accolade from a more cold-eyed source,—reports from two of the best-known investment trusts, containing data on their increased holdings of Merck, Park Davis, Pfizer, and other similar stocks.

Anderson and Priestley of the Mayo Clinic have reported the incidence of infection in CHOLEDOCHAL BILE at the time of operation in the biliary tracts of 100 patients. . . . Seventy per cent had stones in the common duct, and 75.7 per cent of these had bacteria in the bile. Thirty per cent

had no stones, and had only 50 per cent infection. . . . Bacteria are found more often in cases which had previous surgery, and in cases with chills and fever. The organisms are those commonly found in the intestinal tract. . . . They do not believe that infection can be considered a notable factor in the formation of stones. . . . They suggest that antibiotics be used to clear the tract of infection, especially after tubes have been removed.

Probably only a few physicians know or care much about CEREBRAL ANGIOGRAPHY. . . . A sure sign of its progress, however, is a report at a recent x-ray meeting on "LOW-COST Cerebral Angiography". . . . The more it's needed the more it's studied the lower the cost becomes, sure as shooting. And the same in reverse order.

Price and Binns have found demonstrable SINO-BRONCHITIS in 37.7 per cent of a large series of Pittsburgh children who were hospitalized for chronic respiratory symptoms. . . . They tried out four routines of treatment on a later series, and found the best results from a combination of an oral antihistamine, oral or slow-absorption parenteral penicillin, aerosol penicillin, and decongestant-penicillin nosedrops. . . . The nosedrops were required in order that the aerosol could be inhaled thru the nose.

An editorial in the Journal of Pediatrics reminds us that the word 'RESEARCH' comes from the Latin 're' (again) plus 'circare' (to go around). . . . The lower forms of research, in which ideas of others are reviewed or analyzed or appraised, conform to the origin of the word quite well. They are truly a 'go-around'.

FORTUNE Magazine has analyzed the subject of ADRENAL CORTICOID MATERIALS as no medical journal could. . . . Their Science, Economics, and other editors have analyzed the background, the personalities involved, the manufacture, and the future of both American and Mexican drugs. . . . A beautiful article, and one which should give us data from which to predict. It looks like better drugs, new drugs, and lower cost.

TIME Magazine finds interesting THE THEORIES OF DR. REUBEN KAHN, the serologist from Michigan. . . . Dr. Kahn's dreams have been in the same pattern as his test for syphilis,—More diseases should produce some evidence of their presence. . . . The results of the dream and work are now available as a Commonwealth Fund Publication "An Introduction to Universal Serologic Reaction in Health and Disease". . . . The pattern in disease must have a contrast with the pattern in health.

'HOSPITAL TOPICS' (and 'LOOK' Magazine) describe a "Rehearsal for A-Day", at the Massachusetts General Hospital. They have arranged

to move 930 patients into the suburbs as a part of a civil defense plan. . . . In practice they used loud-speakers, moving vans, cars, station-wagons, and volunteer drivers. They 'tagged' staff-members and used them as patients. Teams of nurses and physicians cared for groups. . . . Among the odd pieces of practical information,—station-wagons with mattresses on the floor are not satisfactory vehicles for the seriously ill; almost all of the furnishings of a hospital can be transported in moving vans; and, unless the hospital has 3 hours of warning, it might better have "stood in bed."

A study of 300 unselected surgical patients was made in the anaesthesia department at Harvard to determine the frequency of obvious or silent ASPIRATION OF THE STOMACH CONTENTS DURING ANAESTHESIA. Evans blue dye was placed in the stomach (by gastric tube or a capsule) 15 to 30 minutes before induction. The mouth, pharynx, larynx, and bronchi were inspected after operation. . . . Regurgitation occurred in 26 per cent of the patients, and 16 per cent aspirated gastric contents into the lung. Frank vomiting occurred in only 8 per cent. Aspiration was twice as frequent in the frank emesis as in the silent regurgitation. . . . Regurgitation occurred more often in the Trendelenburg and lateral positions. It was more frequent in the patients handled by inexperienced anaesthetists. Gastric tubes exert a protective effect by reducing the volume of gastric contents.

Dr. Baketel, an editor of 'Medical Economics', says that **THE CHIEF INTEREST OF A PATIENT**

is not in a doctor's reputation, nor in his fee, but in the person who will take the greatest interest in him.

After all the controversy over the THERAPY OF SYPHILIS and neuro-syphilis (which few physicians ever see anymore), it is good to find several definite summaries. . . . E. W. Thomas of New York says that early acute syphilis may best be treated by 1,200,000 units of procaine penicillin in oil and aluminum monostearate on the first day, and 600,000 units per day for five days. Therapy over several weeks has no advantages. . . . Late syphilis (other than CNS disease) may be treated with 600,000 units per day for 15 days. . . . Relapses should be treated with doubled amounts of penicillin. . . . Curtis, Kitchen, O'Leary, Hattner, Rein, Schoch, Shaffner, and Wile say that accumulated experience shows the superiority of penicillin alone, and that heavy metals are unnecessary in the vast majority of cases.

COMING TO TERMS.—

The American Review of Tuberculosis insists that its abstracters use the words 'roentgenogram', 'roentgenography', etc. . . . This is fine tribute to Roentgen, but the whole world now accepts the much simpler 'X-ray', both as a noun and verb.

The tuberculosis, thoracic, and medical societies are all agreed on the usage of 'tuberculous' (adj.—a lesion or infection or condition caused by the tubercle bacillus), and 'tuberculosis' (noun,—disease, caused by the tubercle bacillus). . . . The lexicon of newspapers is stuck with the one (wrong) word, 'tubercular', which simply means 'nodular'.

HUMAN MYIASIS FROM THE SCREWORM FLY IN ARIZONA

(With Report of an Illustrative Case Caused by *Callitroga americana* C. & P.)

John Emmett, M.D., Epidemiologist and Russell E. Siverly, Entomologist*

Infestation of the body with the maggots of flies (myiasis) remains unusual enough to evoke interest in all concerned. Myiasis may be caused by many species of flies and, depending on the species, may occur in the skin, in the genito-urinary and intestinal tracts, in the eye, in and about any of the bodily orifices and in exposed tissue such as wounds and the lesions consequent to syphilis, tuberculosis or epitheliomas.

In 1907 Yount and Sudler (1) collected records of 23 cases of human myiasis which occurred in Arizona within one year and in 1927 Stroud (2) added 16 more seen in 13 years of practice. Records of a hospital in Phoenix show three admissions for myiasis in the past two years. The

disease is more common than the literature would indicate and it is considered timely to present this review and report a recent case in which the causal fly was accurately identified.

Of the 39 Arizona cases, 30 (77%) were nasal infestations. Four occurred in superficial wounds, 2 in skin (axilla and wrist, probably the sites of furuncles), 1 in a carcinoma of the cheek, 1 in a "specific sore" on the cheek, and 1 in an area of gangrene of the heel.

Practically all of the nasal cases suffered from predisposing nasal disease as did the case reported below. Among the diseased conditions reported are epithelioma, chronic syphilitic rhinitis (6 cases), severe chronic rhinitis (etiology unclassified), chronic nasal catarrh, and "an old

*From the Communicable Disease Center, Public Health Service, Federal Security Agency, Phoenix, Arizona.

diseased condition of the nose which had destroyed the septum." Practically all cases, save for the rare accidental inhalation of a blowfly while awake, were infested while sleeping outdoors in the daytime. Males were more commonly affected than females, presumably because of their work. Any age group may be infested, but there is a preponderance of cases among adults of 40 and above.

There were five deaths among the 39 cases, a mortality rate of approximately 13%. All occurred in nasal infestations. Three of the deaths were directly attributable to the depredations of the larvae. (Autopsy on a fatal case recently seen in Phoenix revealed screwworms in both antra, in the sphenoid and ethmoid sinuses, and in the esophagus and stomach.)

The symptoms of nasal myiasis include epistaxis, severe pain, (sinuses, nose, orbital, etc.) nasal discharge, reddening and swelling of mucous membrane and/or the face, fever, restlessness, anxiety and depression. Photophobia and conjunctivitis have been described.

Treatment usually consists of the exhibition of chloroform (from 25% diluted in olive oil to full strength), as sprays, douches or packs. Chloroform stimulates the larvae and facilitates their removal by forceps. The mucous membrane of the nose or soft palate has been incised under local anesthesia and the larvae moving beneath extracted. In cattle, the disease is now treated by a new preparation of the Department of Agriculture called "Smear EQ 335" which is applied topically and contains the larvicide, lindane.

The Arizona cases were "screwworm" infestations ascribed to *Chrysomya macellaria* (Fabr.). The genus is now called *Callitroga* (formerly *Cochliomyia* or *Chrysomya* or *Comptosomyia*) and contains two myiasis producing species, *Callitroga americana* (Cushing & Patton), the primary screwworm fly, and *Callitroga macellaria*, the secondary screwworm fly. The primary screwworm fly was first described in 1933 by Cushing & Patton (3) and it is now believed that most of the infestations prior to 1933 reported as *C. macellaria* were in reality caused by *C. americana*.

Screwworm flies are blowflies, slightly larger than houseflies, with yellow to orange heads, and a metallic, iridescent, blue-green body. The thorax is marked with three distinct, longitudinal, dark stripes. In the United States these

flies are more prevalent in the South and Southwest in the warmer parts of which they may breed all year round. According to Knippling and Travis, continued cold (minimum 20°-47°F, maximum 33°-65°F) kills most if not all adults in nature. Screwworms attack cattle primarily, but horses, sheep, swine, dogs, deer, rabbits, opossums, domestic turkeys, and other animals have been reported infested (4, 5). The female of the primary screwworm fly selects living tissue (wounds) in which to oviposit while the secondary fly seeks carrion. Three and four hundred eggs may be deposited at a time. These are readily visible with the naked eye. Knippling (6) states that the eggs of *C. americana* may be distinguished from those of *C. macellaria* by being whitish and laid in compact, oval, shingle-like masses glued to the edges of the wound or on dried blood clots or scabs. The eggs of *C. macellaria* are more yellowish and less compact. The eggs of both species hatch within a few hours, varying with conditions of temperature and humidity. Each egg yields one larva or maggot which is off-white in color and about 17mm. in length when mature. The dark, pigmented, tracheal trunks of *C. americana* larvae aid in differentiating them from those of *C. macellaria* in which the tracheal trunks are unpigmented. The larvae burrow into the tissues of animal or man on which they feed, reaching maturity in about 5 days. At this time, if possible, escape is made into the ground, it being necessary that the larvae seek a drier medium in which to pupate. In nature the pupae are dark brown to black. Under favorable conditions pupation requires about 9 to 14 days at the end of which time the young fly emerges.

The myiasis seem most clearly classified according to the method of Patton based on the biological requirements of the fly (7). He describes three groups:

Group I

Specific myiasis producing Diptera "whose larvae are found only in living tissue." These are the obligatory parasites hence the most dangerous to animal and man. Here belongs the primary "screwworm fly," *Callitroga americana*.

Group II

Semispecific myiasis producing Diptera which includes those flies that normally breed in dead animal tissue but that occasionally may infest diseased tissues of animals and man. Here be-

longs the secondary "screwworm fly," *Callitroga macellaria*.

Group III

Accidental myiasis producing Diptera, the larvae of which only occasionally and accidentally enter the human body. The house fly is included here and it and many of the other included species may breed in substances used by man as food. They therefore are the usual vectors in cases of gastro-intestinal myiasis but certain species may enter the urethra and bladder and, rarely, may infest wounds and the orifices about the head.

For details of species and of the types of myiasis they cause, the reader is referred to the United States Department of Agriculture publication No. 631, *Flies That Cause Myiasis in Man* by Maurice T. James.

Prevention:

As pointed out by *Dove* (8), the control of myiasis in cattle decreases its incidence in man. There were 55 cases reported from the South-eastern States in 1935, when the incidence of screwworm infestation in livestock was high. The next year when the incidence was low in livestock it was also low in humans, only eight cases being reported.

The proper treatment of chronic nasal disease is most important for this will remove predisposing factors. Protection of open wounds is likewise important. Avoidance of sleeping outdoors in the daytime and the screening of houses to keep out flies obviously are applicable measures. The use of a headnet to prevent screwworm infestation has been suggested but hardly seems practical.

Illustrate Case Report:

The patient is a 70-year-old white male with a long term history of "sinus trouble," recurrent epistaxis and ozena due to atrophic rhinitis. For several years he has sneezed "100 times a day," passing "scabs" from the nose.

On admission to hospital (November 8th) his complaints were uncontrollable nosebleed which had started on the morning of November 6th and severe pain involving the nose and right orbital area. There was associated fever, anxiety and depression. He gave a history of having taken a noon-day nap in his home on November 5th and further recalled having noted a "green blowfly" in the room.

Physical examination revealed an anxious, fe-

brile white male with atrophic rhinitis, ozena and evidence of recent epistaxis. The right side of the face (infraorbital and maxillary areas) was reddened, swollen and tender.

On November 10th screwworm larvae were expressed from the nose during an episode of violent sneezing. With subsequent treatment (direct application of chloroform and local recovery with nasal forceps) an estimated 200-300 larvae were retrieved and the patient made an uneventful recovery. Larvae had invaded the sphenoid sinuses and one eustachian tube.

Specimens of the larvae were identified and confirmed* as being those of the primary screwworm fly, *C. americana*. On November 10th, several of the larvae were placed in soil and pupation occurred during the subsequent 24 hours. Emergence has not occurred in 100 days.

An investigation of the patient's premises and surrounding area was made on November 13th. The patient lived in one of the small aggregation of frame houses in a rural village populated mainly by agrarian workers. There were several head of stock in the neighborhood but no domestic animals on the immediate premises. Some 2 miles east of the patient's dwelling there is a large cattle ranch where screwworm infestation reportedly occurred. With the cooperation of the ranch management an infested steer was examined, and eggs, larvae, and one adult (female) were collected. The eggs were placed on nutrient and blood agar, but failed to develop. The larvae, and the one gravid female were identified and confirmed as *C. americana*.

To recapitulate, larval specimens of *C. americana* were recovered from the nasal passages of the patient. This species is indigenous to the area in which the patient lived, and specimens were collected at a site within normal flight range of *C. americana* from the patient's home (9). In addition, the patient reported dressing a deer at his homesite on November 4th. The resultant odor conceivably attracted blowflies to the immediate area.

SUMMARY:

1. Thirty-nine cases of human myiasis reported from Arizona are reviewed.

2. The relationship of the primary and secondary screwworm flies is discussed, their life cycles reviewed, and Patton's classification of the myiasis cited.

3. A characteristic case is reported in which the causal fly was identified as *Callitroga americana*.

*Acknowledgements:

Grateful acknowledgement is made to Dr. H. R. Dodge of the Communicable Disease Center, Atlanta, Ga., for his confirmation of the identities of larvae and fly; to Dr. J. Brooks of Phoenix, Ariz., for his cooperation in allowing us to study and follow his interesting case; and to Dr. M. Rosenthal of Phoenix for giving us access to his protocol of the autopsy which he performed on the fatal case of myiasis cited above.

BOOK REVIEWS

"Physiology of the Eye: Clinical Application" by Francis Heed Adler, M.A., M.D., F.A.C.S. Pp. 709 with 319 illustrations, 2 in color. Price \$12.50. Published by C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, Missouri. 1950.

The author's long experience as teacher in physiology and ophthalmology at the University of Pennsylvania and his comprehensive knowledge of each of the basic subjects contained in his book, combined with his research ability make him ably qualified for such an undertaking.

Beginning with the eyelids Chapter I, to the final chapter on Binocular Vision, the author's skill and ingenuity portrays his special interest in this field. The chapters dealing with the aqueous humor and the intra ocular pressure well bear that out. Also, Dr. Adler's differential diagnosis of paresis of the superior rectus and the superior oblique muscles make it very clear for the average reader.

This book is most beautifully and instructively illustrated. The bibliography given at the end of each chapter shows how much work the author has done and due credit is given for the help he received from various contributors.

The clinical application of this book in general medicine is well brought out when the author states "one of the characteristic signs of diabetic coma is a very low intra-ocular pressure. The eyes feel mushy soft and the diagnosis can almost be ventured from this sign alone. The low pressure is probably due to an increase of crystalloids in the blood for this is kept fairly constant, an increase in glucose ketonic acid being compensated for by a corresponding loss of chlorides." Another example, the frequent complaint of annoying twitching of the eyelids one encounters in the practice of ophthalmology, the author advises small doses of quinine for this

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spasm.

Dr. Adler's style and methods of presentation of the twenty-two chapters, arranged in a conventional sequence with such a degree of clarity, make this an excellent text and one which can be highly recommended.

H. J. French, M.D.

"Principles and Practice of Surgery." By: Jacob K. Berman, A.B., M.D., F.A.C.S., Associate Professor Surgery, Indiana University School of Medicine, Indianapolis, Indiana. Cloth \$15.00. Pp. 1378 with 429 illustrations. The C. V. Mosby Co., 3207 Washington Blvd., St. Louis 3, Missouri. 1950.

This excellent volume appears to have well filled its aim of correlating the basic sciences to the fundamental principles of surgery, and can accordingly be highly recommended as a text for students, as well as a fine completely new abbreviated reference for the busy general surgeon.

Its arrangement is in five sections:—General Considerations of Surgical Principles, Local Response and General Body Reactions to Injury, General Reactions to Injury, Reactions of Tissues and Organs to Trauma of Unknown Origin, and lastly Diseases and Injuries of Specific Organs and Systems."

It is refreshing to find a textbook rather well represented in all the newer surgical fields such as in cardiac and blood vessel surgery; also such operative techniques as vagotomy are covered.

While some might question discussion of the gallbladder and bile ducts under the gland section instead of the alimentary section, it is well covered with the liver and pancreas.

On the whole then this is an extremely fine new textbook of general surgery well organized and arranged and with ample references given so that the student may pursue each subject further. It is highly recommended.

W. H. C.

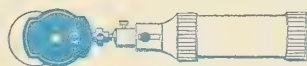
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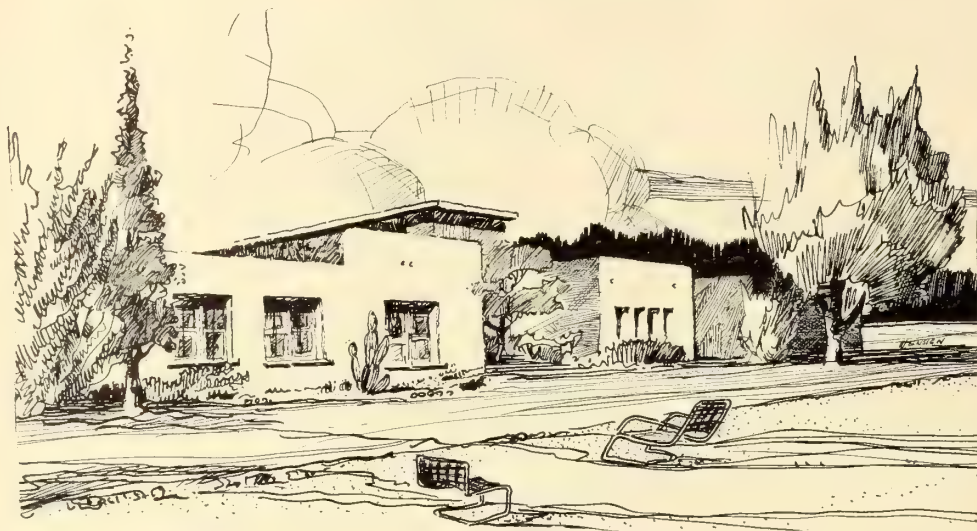
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NEWS ITEMS

Do you know that the National Board voted a scholarship of \$500.00 to the Careers for Nursing, and that the auxiliary delegates voted at convention to contribute \$10,000. to the National Fund for Medical Education, and \$100 to the World Medical Association?

—o—

A revised list of "Sources of Motion Pictures on Health" has been prepared by the Committee on Medical Motion Pictures of the American Medical Association. This new mimeographed list includes 9 pages of addresses of the major loan and rental libraries, the state health departments' film libraries and references to printed lists and catalogs. Copies are available from:

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535 North Dearborn Street
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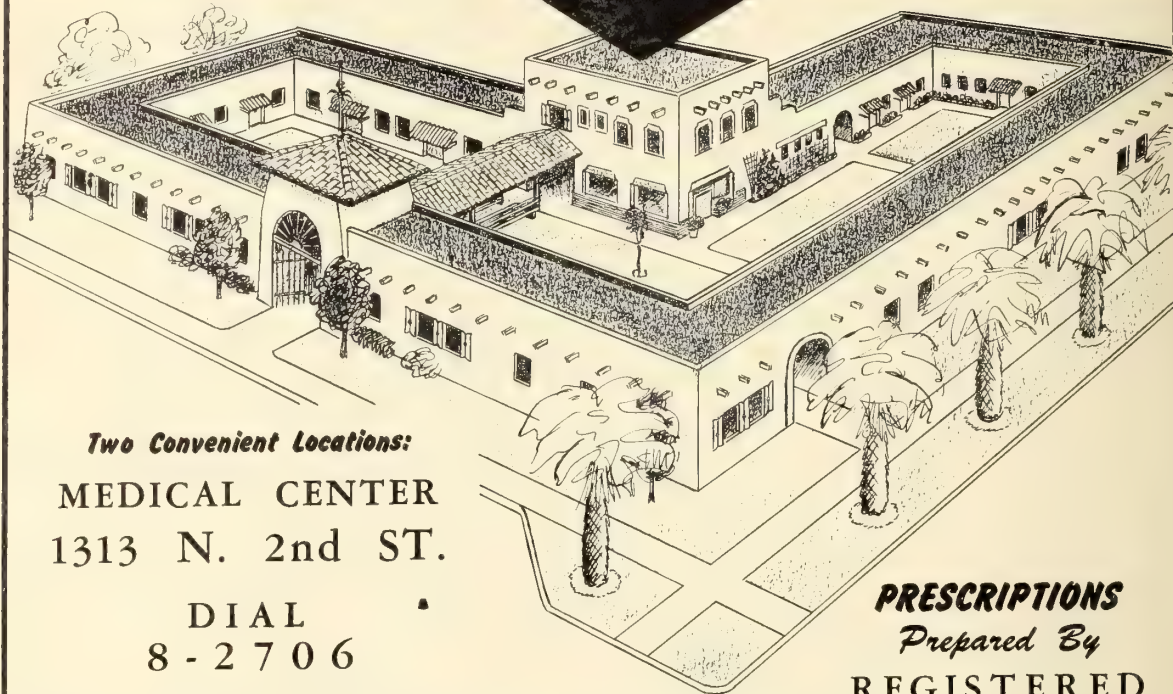
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What is Civilian Defense? It is just what it sounds—civilians who have banded together to defend and protect themselves from an attack or disaster. As the world situation stands today, civilian defense should be supported by more than a few individuals who are far-sighted enough to see the tremendous job of organization involved—it should be supported by all of us working together. Should atomic war suddenly explode in our faces, which we devoutly hope will not happen, the Red Cross, the hospitals, and our medical societies will all call upon us to help them. To be of use in such an emergency we should be prepared.

First, let me give you a blue print of what has been done. The United States government has spent much time and money on writing the ideal civilian defense setup. It has compiled the research of its army medical department, and evaluated the defense efforts of England and other European countries in the last war. These have all been sent to the governors of the individual states. The A.M.A. has compiled a tremendous amount of material from studying the reports on what happened to the population of Hiroshima. The A.M.A. has figured what health and emergency services we would need, if subjected to atomic attack, and how many volunteers are necessary to run such health services. These reports have been sent to all the medical societies in the country.

At this writing, the governor of Arizona has appointed Mr. George B. Owen, in Phoenix, state civilian defense director. He, in turn, has appointed a special staff of ten people to coordinate the efforts of the state. In charge of health is Dr. Joseph M. Greer, assisted by Dr. C. G. Salsbury. These are all recent appointments, and the organization is just starting. As Arizona is not designated a primary target—in other words a place where an atom bomb is likely to be dropped—we have been slower than some of the coastal and industrialized states in organizing. The wheels are now beginning to turn, and while waiting for an appointed role, we can also become ready.

We can become informed in what can be done to protect ourselves in an atomic attack. It is possible to protect yourself; you don't have to close your eyes and go around hoping that it just won't happen here. There is an article in LIFE magazine, which the editors are glad to send anyone for a few cents, which outlines very simply a few basic steps anyone can take to protect himself. The NEW YORK TIMES also has a pamphlet of reprints, from a series of articles it published, entitled "We Are Not Helpless," which they will send you for ten cents. Your medical society has many articles which give important information, although in somewhat more technical terms. By reading these throughout the Auxiliary membership, we can become informed, and thereby help prevent a disastrous panic should an attack actually occur.

Investigation has disclosed that one of the causes for large numbers of casualties at Hiroshima was the lack of common knowledge of first aid. The many articles I read all stressed the importance of everyone knowing first aid, especially for flash burns. Here is something all the members of the Auxiliary and the members at large can do—become proficient first aiders. If you had a course in the last war, renew it; if you have not had a course, your local Red Cross organization will be happy to furnish an instructor.

Many additional nurses and nurses aides would be needed immediately, should atomic warfare reach our shores. There may be nurses in the Auxiliary who have not practiced their profession since they were married; these could offer their services should an emergency arise, or become members of the Red Cross teaching staff. Some, who may have let their certificates lapse, could renew them and then would be in a position to help in the same way. Those of us who have not had nurses training could take advantage of the excellent courses which the Red Cross give and become nurses aides or home nurses.

There are several movies on the atom bomb and atomic bomb defense which it would be possible to obtain, either through writing your state medical society or the civilian defense director. These might be a good way to interest the membership in civilian defense.

If you are a member at large, wishing to be of service to your community, your state director of civilian defense stands ready to offer sug-

gestions to you. If you are a member of a county auxiliary, your medical society will have a doctor in charge of civilian defense. Contact him. At all times your program chairman will be glad to offer any assistance possible. Remember, however, that the important thing for us, as doctor's wives, is to prepare ourselves and assist our communities to the best of our ability.

POLIO POINTERS FOR 1951

Reprinted in part from the BULLETIN—

If Polio comes—

DO Allow children to play with friends they have been with right along. Keep them away from new people, especially in the close daily living of a home.

Because—Once polio has appeared in a community, scientists say the virus probably is wide-spread. Your children probably have come in contact with it already and developed a degree of resistance to that particular virus.

DO Wash hands carefully before eating and always after using the toilet—especially important when polio is around. Also keep food clean and covered.

DO Watch for signs of sickness, such as headache, fever, sore throat, upset stomach, sore muscles, stiff neck, extreme tiredness or nervousness, trouble in breathing or swallowing.

DO Put a sick person to bed at once, away from others, and call the doctor. Quick action may lessen crippling.

DO Telephone your local Chapter of the National Foundation for Infantile Paralysis, if you need help. Locate through telephone book or health department. No patient need go without care for lack of money. Your Chapter will pay what you cannot afford. Because—The 2800 local chapters of the National Foundation, supported by your contribution to the March of Dimes, exist for this purpose. Other March of Dimes funds are spent for scientific research and the training of much-needed personnel.

DO Remember, at least half of all polio patients get well without any crippling.

Because—Recent surveys show that 50% of all diagnosed polio cases suffer no paralysis at all. Another 25% recover with no disabling after-effects. 15% are severely paralyzed, and about 8% die.

DON'T—get over-tired by hard play, exercise, work, or travel. This means men, women, and children.

DON'T—get chilled. Don't bathe or swim long in cold water, or sit around in wet clothes.

DON'T—have mouth or throat operations during a polio outbreak.

DON'T use another person's towels, dishes, tableware, or the like.

DON'T—take children to places where there is polio.

DON'T—take your child out of camp or playground, where there is good health supervision.

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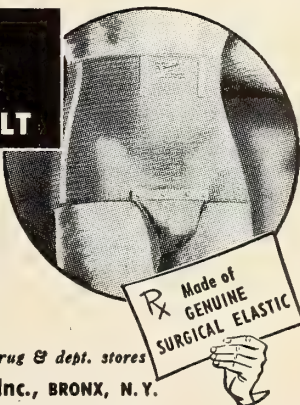
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IF YOUR A.M.A. JOURNAL IS MISSING

Recently the Executive Office of the Society has received a number of telephone calls from members asking the question, "I haven't been receiving the J.A.M.A. for the last few weeks. I sent in my check for \$25 for A.M.A. dues on such-and-such a date. What has happened?"

Investigation reveals that these calls usually are from members who did not pay their 1950 A.M.A. dues by the deadline date of December 31, 1950, and who have since sent in their checks for 1950 on say—January 15, 1951.

What has happened is quite simple. When the 1950 dues were not paid by the end of the year the doctor entered the category of delinquent membership in the A.M.A. His name was removed from the roster of members and his name was removed from the list of those who receive the Journal of the A.M.A.

Such delinquent members will not be entered on the circulation list of the Journal of the A.M.A. until they have been reinstated to full membership. This means they must pay BOTH their 1950 and 1951 dues. If they have now paid their 1950 dues (after Jan. 1, 1951) they must also pay the 1951 dues before they enter status of member in good standing. Until then they will not receive the Journal.

Word direct from the A.M.A. is that members who paid their 1950 dues on time (before the end of the year 1950) are in good standing and have until the end of 1951 to pay their 1951 dues. They are considered as 'good circulation risks' and will continue to receive the Journal during 1951 even if they cannot pay their 1951 A.M.A. dues until later this year.

BUT members who did not pay their 1950 dues on time are now delinquent. They are not considered good circulation risks and the Journal will not be sent to them until they enjoy full reinstatement by paying both 1950 and 1951 dues.

It was explained in the circular which accompanied the bills for A.M.A. dues that both 1950 and 1951 dues must be paid. The penalty for those who did not read this, did not believe it, or did not act upon this advice is the penalty of not receiving the Journal of the A.M.A.

When a member pays his full dues and is reinstated in the A.M.A. his subscription to the Journal will start again. And the reinstated member can write directly to the Office of the

J.A.M.A. and ask for back copies that he has missed.

We are informed that the Journal printed a number of extra copies of the early issues of 1951 to cover just this possibility. But the extra supply is limited and there can be no guarantee that the supply will not be exhausted.

To repeat the main point:

A.M.A. members who paid their 1950 dues during 1950 have no need to worry. Their J.A.M.A. will keep coming to them throughout the year. But they must pay their 1951 A.M.A. dues during 1951, quite naturally.

Members who have not paid their 1950 A.M.A. dues until after January 1, 1951, are temporarily NOT receiving the Journal and this is one of the penalties they pay for being delinquent.

Already a few calls have come from delinquent members who have now paid their 1950 and 1951 A.M.A. dues and cannot understand why they do not immediately receive the A.M.A. Journal the following week after they write out their checks. To these physicians it may be of interest to know something of the process of reinstatement.

For example, thousands of checks from members come to the County Society for payment of A.M.A. dues. After opening the envelopes and sorting out the checks, the proper amounts must be entered upon individual treasurer's cards for the permanent records. Lists of names of members paying dues must be arranged in alphabetical order for the auditors. Each check must be stamped for deposit, and deposit slips filled out and rechecked again. The money for A.M.A. dues thus enters the bank to the account of the County Society.

All these operations, including still others, are simultaneously going on to record the payments for County and State dues which are handled separately.

Following such activity at the level of the county society alphabetized lists of members who have paid their A.M.A. dues are sent to the Medical Society of the State of New York together with a check to cover payment of such dues. The State Society, in its turn, must enter the information on its cards, prepare audit lists, make deposits and maintain its own set of records.

Next the State Society sends to the A.M.A. lists of members who have paid their A.M.A.

dues and sends covering checks for each such list.

In its turn the A.M.A. must enter all information on its own cards and—along the way— notifies the A.M.A. Journal that member X, for example, is now in good standing. If member X's name has been removed from the mailing list of the J.A.M.A., because he was delinquent, a new addressograph plate must be prepared with his name and address so that labels can be

printed to mail his magazine. Since these labels are prepared an issue or two ahead of mailing it thus takes several weeks to start the machinery flowing again at the Journal office.

All these steps—at the county level, at the state level, and at the national level—provide an explanation of why it is impossible to expect that as soon as a check is mailed to the N. Y. County Medical Society the Journal of the A.M.A. will arrive the next week.

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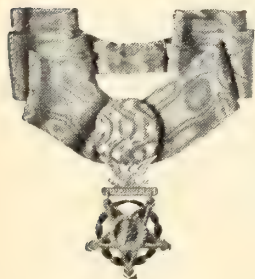
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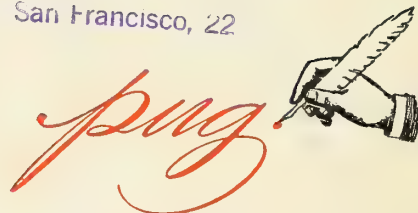


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- 1 Adams, C. H., and Cecil, R. L.: Ann. Int. Med. 33:163, 1950.
2 Bayles, T. B.: Medical Forum, Mod. Med. (no. 24) 18:86, 1950.
3 Gilbert, J. T., Jr., and Moore, F. H.: J. Kentucky State M. A. 48:308, 1950.

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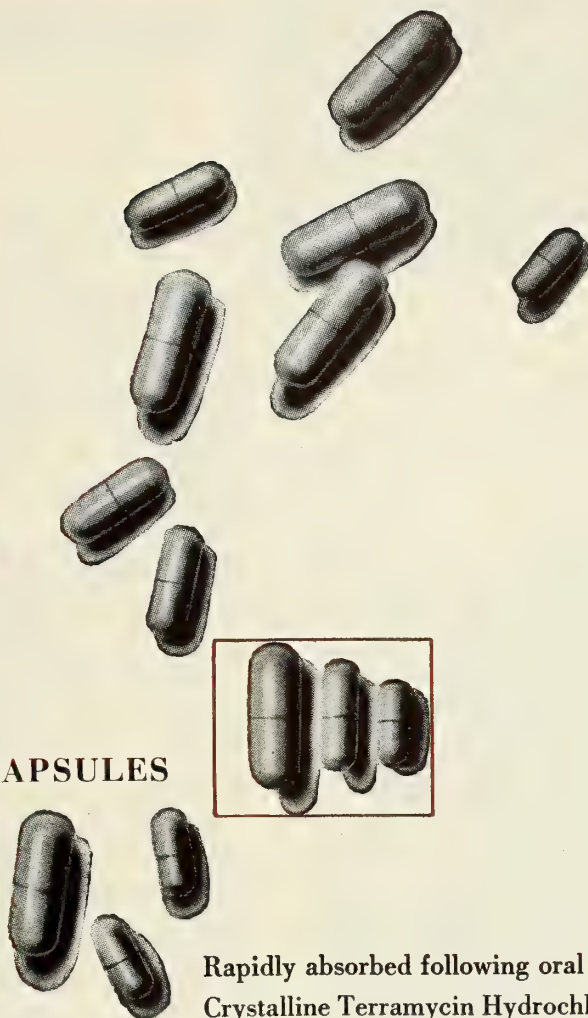
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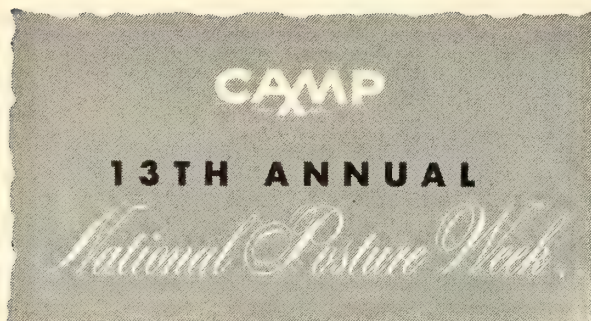
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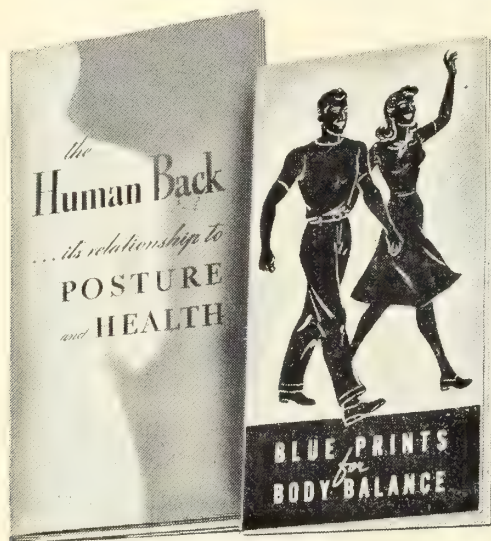
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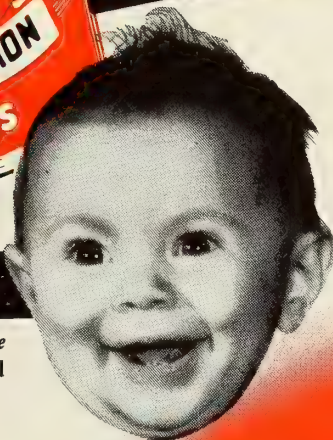
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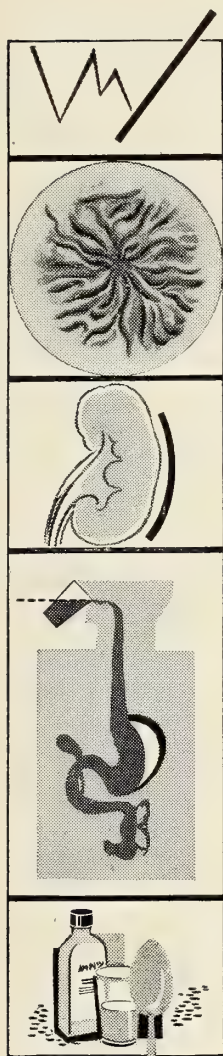
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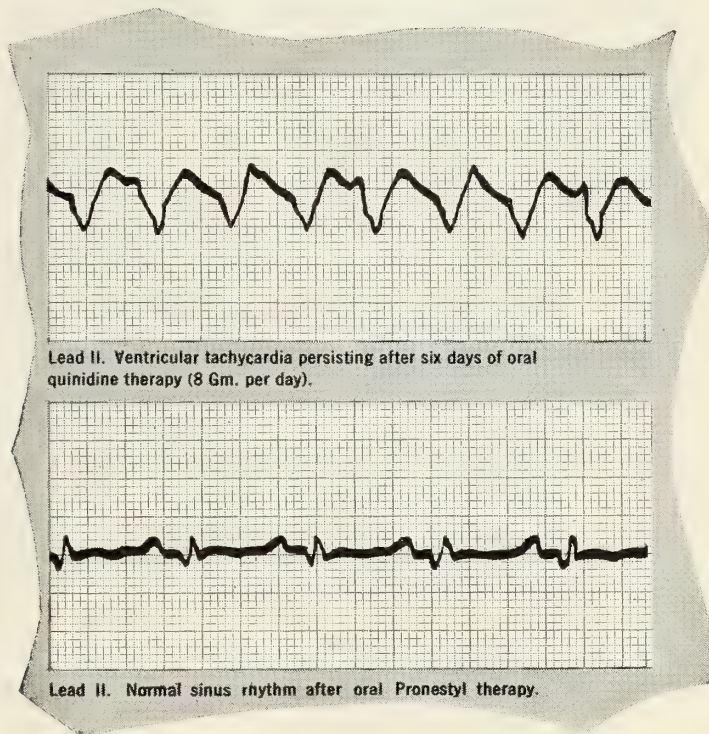
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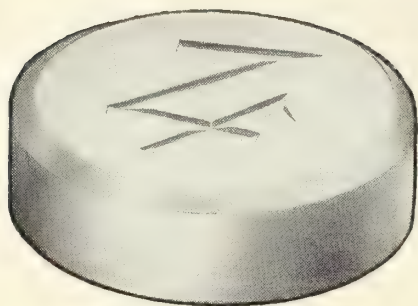
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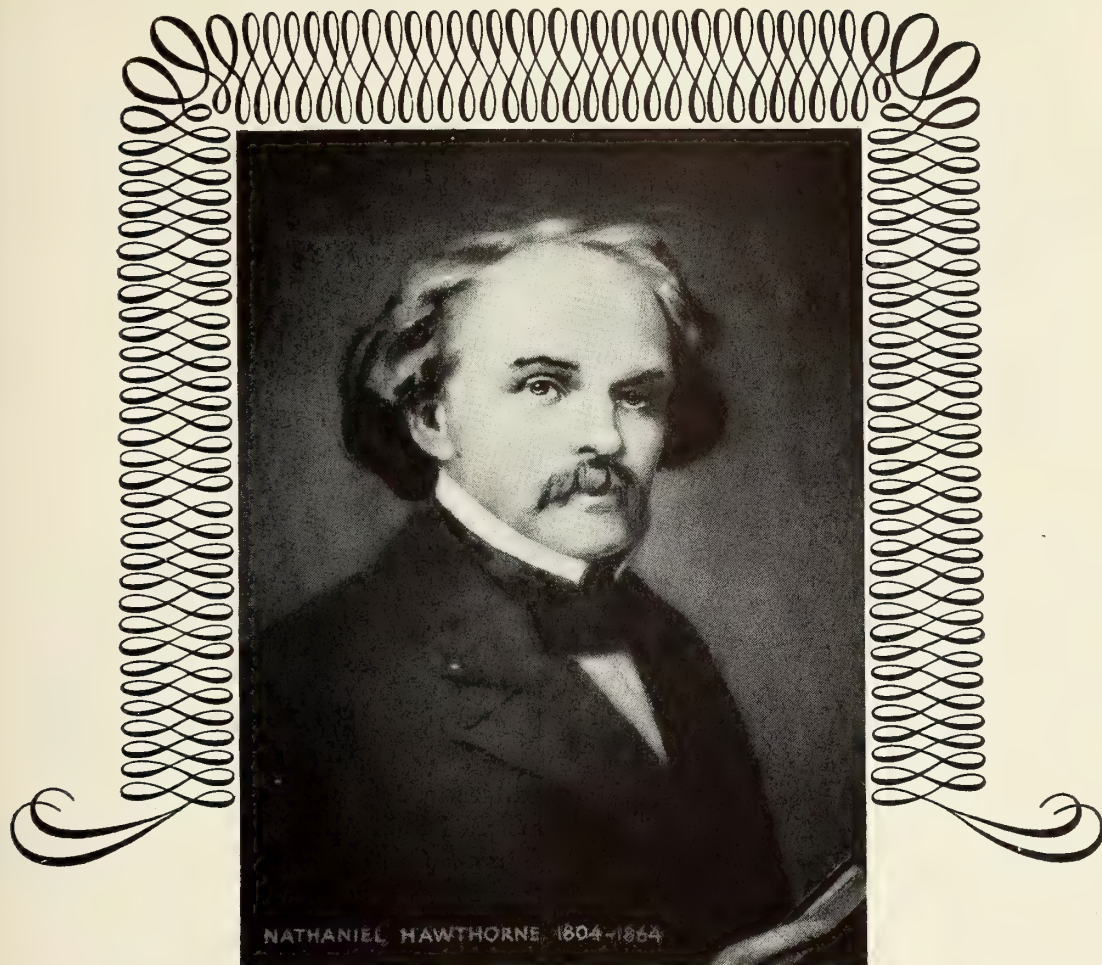
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Relationship of Stress to Autonomic Lability

Studies in psychosomatics have shown that functional disorders often are a result of the patient's inability to adjust to emotionally stressful situations (stressor factors).

Nervous tension and chronic anxiety, discharged through a labile Autonomic Nervous System, can cause somatic disturbance.^{1,2} Such states may involve any one of the organ systems or several at one time.^{1,3} The outline below is designed to relate gastrointestinal and cardiovascular symptomatology to the exaggerated response of the autonomic nervous system.

	Physiologic Effects of Autonomic Discharge	
	Sympathetic	Parasympathetic
Gastro- intestinal System	Hypomotility Intestinal Atony Hyposecretion Reduced salivation	Hypermotility Gastrointestinal spasm Hypersecretion
Cardio- vascular System	Rapid heart rate Peripheral vaso- constriction	Slow heart rate Vasodilatation
Functional Manifesta- tions	Palpitation Tachycardia Elevated blood pressure Dry mouth and throat	Heartburn Nausea-vomiting Low blood pressure Colonic spasm

The data here tabulated is from references 3,4,5,6,7, given below.

When the clinical picture is suggestive of functional disorder, the diagnosis is supported by the presence of the following indications of autonomic lability:

Variable Blood Pressure
Body Temperature Variations
Changing pulse rate
Deviations in B. M. R.
Exaggerated Cold Pressure Reflex
Oculo-Cardiac Reflex Abnormalities
Glucose Tolerance Alterations

Therapy in these cases is directed toward: 1) relieving the somatic disturbance to prepare the patient for psychotherapy*; 2) guidance in making adjustment to stressful situations and correction of unhealthy attitudes.

*Drug treatment using adrenergic and cholinergic blocking agents in conjunction with sedatives.^{8,9,10.}

1. Baugh, F.: Postgrad. Med. 4: 208, 1948. 2. Wilbur, D.: J.A.M.A. 141: 1199, 1949. 3. Williams, E. and Carmichael, C.: J. Nat'l. Med. Assoc. 42: 32, 1950. 4. Goodman, L. and Gilman, A.: The Pharmacological Basis of Therapeutics, The Macmillan Co., 1941. 5. Katz, L. et al: Ann. Int. Med. 27: 261, 1947. 6. Weiss, E. et al: Am. J. Psychiat. 107: 264, 1950. 7. Alvarez, W.: Chicago Med. Soc. Bulletin, 581, 1950. 8. Rakoff, A.: A Course in Practical Therapeutics, Williams and Wilkins, 1948. 9. Karnosh, L. and Zucker, E.: A Handbook of Psychiatry. C. V. Mosby Co., 1945. 10. Harris, L.: Canad. M.A.J. 58: 251, 1948.

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ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 10



OCTOBER, 1951

ORIGINAL ARTICLES

NODULAR TUBERCULOSIS OF THE LUNG*

JOHN S. CHAPMAN, M.D.

Dallas, Texas

Under this title it is my wish to discuss two specific aspects of pulmonary tuberculosis. Although these two conditions differ roentgenographically, from the morphologist's standpoint the most significant point of their divergence is in their size and number. The first aspect of nodular tuberculosis is manifest usually as small, rounded, fibro-caseous shadows which are well circumscribed and are usually located relatively high in one or both apices. The other nodular form more frequently is larger, perhaps of a diameter of two or three centimeters, most frequently single and located in almost any part of the lung where tuberculous cavitation occurs. Such a nodule is sometimes called a tuberculoma or sometimes a tuberculoma-like filled-in cavity. Its origin, however, is the result of obstruction of the draining bronchiole. After this, liquid material fills the hiatus to produce a solid shadow; still later the contents gradually become inspissated. While such a change has been referred to in the past as a variety of cavity closure (4), it seems that a more proper and accurate term, which would also be morphologically correct, would be cavity obturation. This term is also of convenience in distinguishing such a nodule from a true tuberculoma with its characteristic onion skin lamellae.

Though in their familiar roentgenographic aspect they may seem somewhat dissimilar, I hope to be able to show on morphologic and clinical grounds that the difference is quantitative rather

than qualitative and to infer from this similarity what appears to be a proper treatment for the one will also be rational treatment for the other.

Pathologists (5,6,8) among whom perhaps the most recent is Medlar, have shown repeatedly that the apical and subapical nodules mentioned above are nothing but hiatuses of small size which are filled with a material that varies all the way from the consistency of a paste through that of dense cheese to perfectly solid, gritty material. Such nodules, though they are more familiar to us in the apical regions, may nevertheless be found in almost any location in the lungs when postmortem study is undertaken. The wall of these small structures is composed of dense, hyalinized connective tissue in the older nodules, while in the younger ones the fibrous tissue is relatively immature and still to some degree vascularized. In many instances the wall is quite thin, while in others it may be as much as two or three millimeters thick. Proximity to bronchioles varies.

In the cases with large nodules, the result of cavity obturation, the histologic picture is almost identical except as the size or the location may be of some degree of interest. Here the wall is composed of fibrous tissue of almost any age from the earliest fibroblastic proliferation to dense hyalinized scar. The thickness of the wall likewise varies rather considerably, but in these lesions it is more common for the walls to be slightly thicker than in the smaller nodules. The contents are essentially the same, except that in these larger nodules calcification is perhaps less frequent. Living organisms are present

*Read before Sixtieth Annual Meeting, Ariz. Med. Assoc., April 30, 1951.

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in the walls of both, except possibly in very old lesions.

There is perhaps a difference in the pathogenesis of the nodules. The smaller appear to arise either from hematogenous or bronchogenic seeding. In the first instance there is not necessarily a close communication with a bronchus. It is probably also true that not all of these small nodules underwent a cavitory phase, but rather appeared first as small areas of exudation which subsequently underwent caseous necrosis, becoming encapsulated before bronchial drainage occurred. Others unquestionably may have a cavitory phase—a condition familiar clinically as the so-called “moth-eaten” rarefactions.

The development of the single larger nodule through cavity obturation has already been mentioned, but it may be added that it seems theoretically possible—and I believe I have seen the clinical demonstration—that a large area of exudation may undergo partial reabsorption and partial caseation without ever achieving the bronchial discharge which would reveal the lesion as a cavity. Such a change from an exudative to a nodular lesion without the intermediate stage of cavity was particularly common in the days of pneumothorax, when predominantly exudative lesions were placed under collapse before frank cavitation had occurred but significantly and undoubtedly after caseation was well under way. The suggested view is that collapse produced a rapid reabsorption of the exudative component and that it also prevented or decreased bronchial drainage with necrotic material being retained and encapsulated.

It should be emphasized at this point that whether the nodule is relatively large and single or quite small and multiple, it represents an attempt at healing. The lesion or lesions are firm and inelastic, their walls are fibrous and their contents are excluded temporarily or permanently from the bronchial tree, the circulation and the contiguous tissue. Patients, if they have no other lesions than these, present satisfactory clinical evidence of arrest in the form of X-ray stability, negative bacteriologic studies, normal sedimentation rates and blood counts, and absence of constitutional symptoms. In the past it was necessary to be content with this result. Since this necessity arose from the fact that no method of collapse nor any amount of bed-rest seemed to alter the lesions significantly dur-

ing considerable periods of observation and since it is now possible to apply other measures, the most imperious demand is made upon us to decide whether or not we should now be content with our treatment when we have reached such a stage. Day and associates (2) question the safety of such lesions.

Recently it has been stated in the literature (7) that obturated cavities have a very satisfactory prognosis. Since local experience seemed to cast some doubt upon this statement, it was decided to restudy a group of private patients who had in common a single characteristic, namely that they had apparently been ready for classification as quiescent or, in some cases, even fully arrested but subsequently developed a reactivation of disease. This study was begun in 1943 and includes patients who received several diverse forms of therapy. The original intent of this special grouping was to serve as a check upon my judgment in the selection of the treatment. Eighteen patients who at one time were on the way to recovery but who later had reactivation are used in this analysis. The accompanying table indicates as objectively as possible the nature—for this discussion, not the cause—of the reactivation.

TABLE I

Nature of Reactivation in a Group of Patients who had achieved Quiescence or better.

Exudative nimbus	7
Evacuation of nodule	6
Seedling nodule	1
Hematogenous	2
Dissemination from Diseased Bronchus	2

Two patients were classified as having had hematogenous dissemination. One was a female in which a pneumothorax which had been carried to a successful completion without any local evidence of recurrence but who after some fifteen months of graduated bed-rest developed tuberculosis of the cervical glands and papulonecrotic tuberculids of the skin. The other was so classified because after having achieved a very satisfactory result upon one side he later showed a cluster of nodules high in the apex of the other lung. In one patient it was not possible to determine what type of spread took place. Two patients apparently developed a spread of their disease from lesions located within the bronchus of the major side. The remaining thirteen patients all formed nodular lesions. Of these six

apparently suffered reactivation as a result of the development of bronchial communication while six others seemed to be reactivated as the result of an exudative flare around previous nodules. It is of interest that this group comprises patients recently managed and that in many such reactivation seemed to result from the cessation of streptomycin or pneumoperitoneum therapy. This group is marked by the fact that they were on the whole less stable, or were stable for a much shorter time, than the others. The thirteenth patient simply presented a new nodule below a pre-existing cluster, without there having been definite evidence of renewed activity about the older lesions. Pathologic studies failed to distinguish the more recent nodule from the others.

Both the old and the recent nodules showed a tendency to slough out leaving behind open cavities. In some of the cases the cavity had preceded the formation of the nodule, while in others no roentgenographic observation of a cavity was present. The appearance of the seedling nodule, so far as observed, has been limited to a single case in which there was already multiple nodulation, while the development of the exudative nimbus, at least so far as I have been able to observe, has likewise been confined to multiple nodulation.

Medlar's (5) recent contribution in which he presents very clearly the concept of revascularization of the nodular lesion seems to be an adequate explanation of the succession of events. In the one case, in spite of a practically hyaline wall, a softening took place between the nodule and a bronchiole, while in the other the incompletely organized wall seemed to leak organisms out into the adjacent tissue with a corresponding inflammatory reaction. That this exudative nimbus is not often encountered around an obturated cavity may well be due to the fact that the limiting wall is fairly firmly organized, whereas the obturating plug of fibroblasts, being relatively newer, is more subject to revascularization.

It is my opinion that this study shows, that both multiple nodulation and obturated cavities are prone to reactivation. In this relatively small series they behave with considerable similarity. It is not to be concluded that all such cases or even a large per cent reactivate. The significant point is that of all reactivations in this small series revascularisation of nodules or ob-

turated cavities accounts for 65-70 per cent of the cases.

In a larger group we have, recently, frequently been advising surgical removal of obturated cavities. In a few cases sub-segmental resection has been sufficient; in more it has seemed better to do a segmental or even a lobar resection. Up to the present in this group there have been no early (up to 2 years) unfavorable results. The thesis has been that at least among the patients we have seen the chance of re-opening of a filled-in cavity has been great enough that we have been unwilling to accept such a lesion as a satisfactory end result of treatment. Since no form of collapse can have too much effect upon such lesions their ablation seems the logical step.

If this reasoning is true of obturated cavities, it should perhaps likewise be extended to the clustered nodular disease of the apex which presents the same obstacles to successful collapse therapy and which certainly in this series seems to possess a rather high reactivation potential. This is not now regarded as a regular indication for resection (1, 2, 3), and admittedly such an attitude is radical; certainly for the present resection should be limited to those patients in whom the nodular disease has caused at least one reactivation. There is one further reservation that derives from the patient in whom a seedling nodule appeared. If that nodule instead of being a local lymphatic spread or merely a spread by continuity of tissue should instead represent a new hematogenous deposit resection is indefensible.

Finally some explanation has been offered for the highly obstinate behavior of apical nodular disease which Dr. Amberson has very vividly described as browsing downward. Perhaps, also, this shifts away from both patient and physician a little of the onus for the behavior of the "indolent" lesion. Possibly its resistance to treatment is at least partly a fact and not entirely the result of an inadequate physician or an uncooperative patient.

SUMMARY

1. A series of private patients has been studied with the intention of determining the cause of reactivation.

2. In 65-70 per cent of the group renewed activity of the tuberculosis seems to have been the result of the revascularization of nodular lesions or obturated cavities.

3. It has been shown that both multiple small nodular lesions and obturated cavities behave with considerable similarity.

4. It is suggested that resection of the clustered nodules may be considered under special conditions:

- a. When it is understood that this resection is undertaken purely as a prophylactic measure after full control of tuberculosis has been accomplished.
- b. When there has been at least one and preferably more than one episode of renewed activity.
- c. When future evidence does not establish

that repeated hematogenous seeding is responsible for a significant number of re-activations.

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PARTIAL PULMONECTOMY*

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Partial pulmonectomy is used to designate the following operations; (a) lobectomy, (b) bilobectomy, (c) segmental pulmonary resection, (d) local excision of pulmonary tissue and, (e) cavity enucleation. Partial pulmonectomy is therefore excisional pulmonary surgery, but for the purposes of this paper it does not include pneumonectomy. This operation has been used in the treatment of bronchiectasis, tuberculosis and coccidioidomycosis, plus one case each of emphysematous bleb and gunshot wound.

SUMMARY OF SURGICAL RESULTS

The first chart depicts the results in bronchiectasis and tuberculosis. There were thirty-four operations for bronchiectasis. Lobectomy was performed in thirty-one cases, bilobectomy in two cases and segmental resection in one case. There was one death during surgery, due to cardiac arrest. There were twenty-two operations for tuberculosis. Lobectomy was performed in seventeen cases, bilobectomy in two and segmental resection in three cases. There were no deaths in this group of patients. The cases designated as cured were those individuals who had returned to normal activities for a period of at least one year, and whose sputum, gastric smears and cultures had been negative repeatedly during that time. Those individuals listed as possible cure had negative studies, but who had been observed less than one year and who had not returned to normal activities. With one exception all individuals in this group

received streptomycin and/or para-aminosalicylic acid before and after their surgery.

CHART 1

Bronchiectasis		Tuberculosis	
Total Cases—34		Total Cases—22	
Cured (23)	67%	Cured (7)	32%
Exp. Cure (2)	6%	Poss. Cure (9)	41%
Improved (5)	15%	Improved (2)	10%
	88%		83%
Unimproved (3)		Unimproved (1)	
Worse (1)	12%	Worse (3)	17%

The second chart depicts the results in coccidioidomycosis. Lobectomy was performed in four cases, segmental resection in two, local excision in two and cavity enucleation in one case. Particular attention is called to the one case marked unsatisfactory. Following lobectomy the patient developed a broncho-pleural fistula complicated by empyema. Open drainage of the empyema followed by extensive thoracoplasty resulted in closure of the broncho-pleural fistula and obliteration of the empyema space. Thereafter a chest wall infection persisted. For over two years unsuccessful attempts were made to eradicate this chest wall infection. Curretage of the sinus tracts was ineffectual. She also received X-ray therapy, and chemotherapeutic and antibiotic drugs. She has received prodigiosin intravenously and locally. Prodigiosin caused her a good deal of discomfort due to phlebitis and high fever but had no effect on the coccidioidomycosis. Streptokinase and streptodornase locally was ineffectual. This one case is enough to emphasize the fact that coccidioidomycosis may occasionally prove to be a very difficult problem.

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CHART 2
COCCIDIOIDOMYCOSIS

Indication	Operation	Complic.	End Result
1. Cavity Infection Hemorrhage	Local Excision	0	Cured
2. Large Cavity	Lobectomy	0	Cured
3. Cavity Infection	Segmental Resection	0	Cured
4. Cavity Infection	Enucleation of Cavity	0	Cured
5. Cavity Sp. Pneumo. Empyema	Lobectomy Decortication	+ Partial Stenosis Middle Lobe Bronchus	Improved
6. Large Cavity	Lobectomy	+ + B. P. Fistula Empyema	Unsatis.
7. Cavity Sp. Pneumo. Empyema	Thoracotomy Cavity Enucleation Decortication	0	Cured
8. Tumefaction	Local Excision	0	Cured
9. Tumefaction	Local Excision	0	Cured

The third chart is a summary of all cases. Partial pneumonectomy was performed in sixty-seven cases with one death.

DISCUSSION

Experience gained from this group of cases has led to some observations worthy of recording. Probably the most important observation has to do with the position of the patient on the table. Some thoracic surgeons and anesthesiologists are convinced that it makes no difference what position is used. Such was the conviction of the author in the beginning of this series of partial pneumonectomies. With increasing experience a definite preference for the face-down position has resulted. Particularly in large individuals, in individuals of questionable respiratory reserve and in individuals with excessive secretions it is now considered obligatory. There is no doubt the patients withstand a prolonged procedure much better. Furthermore it is less fatiguing to the surgeon from a technical standpoint.

CHART 3
PARTIAL PNEUMONECTOMY

Indication	Excisional Surgery in Sixty Seven Cases	Number	Deaths
Bronchiectasis		34	1
Adenoma-1: Broncholith-1			
Lung Abscess-1			
Tuberculosis		22	0
Carcinoma-1			
Coccidioidomycosis		9	0
Emphysematous Bleb		1	0
Gun Shot		1	0
(Transection of the Lingular Bronchus left upper lobe)			
Total Cases		67	1

Another observation which may be common knowledge but is seldom emphasized has to do with sustained hypertension. Interruption of the operation should be practiced routinely when the systolic blood pressure is maintained at an

abnormally high level for as long as ten minutes. If the anesthetist cannot correct this within a second ten minute period, then the operation should be abandoned. Such an occurrence means cerebral anoxia and/or an increase in the carbon dioxide tension of the arterial blood. Continuation of the operation in the face of such danger signals is inviting disaster.

Persistence of positive sputum, in cases of tuberculosis following pneumonectomy may be due to ulceration around the sutures used to close the bronchus. On two occasions removal of the sutures through the bronchoscope resulted in prompt healing of the stump and a conversion to negative sputum.

CONCLUSIONS

The operation of partial pneumonectomy is a safe procedure, but the results must be qualified according to the disease for which the survey is performed. Results are herein recorded showing a cure of the greater portion of individuals with bronchiectasis and coccidioidomycosis by surgery. Partial pneumonectomy for tuberculosis cannot be accurately evaluated in the immediate postoperative period. This operation does not ordinarily result in removal of the entire diseased area. At best the surgeon removes only the largest or most active focus of infection. Despite what help the patient may receive from streptomycin and allied drugs, it is evident that the patient's immunologic forces must still play the major role in overcoming and holding the remaining tuberculosis in check. Those who are eventually classified as cured must be so classified only after careful and prolonged follow-up studies.

SOME PROBLEMS OF INTESTINAL OBSTRUCTION

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Intestinal obstruction, in spite of advances in diagnosis and management, remains one of the most serious problems in surgery.

The incidence of obstruction remains high. Although a high salvage rate from peritonitis of various causes has now been attained, these same salvaged patients at a later date, constitute a larger group in whom intestinal obstruction, particularly from bands and adhesions, may be expected to occur.

The high incidence and the great variety of causes of intestinal obstruction was noted in a survey completed by the author (1) in 1947, as shown in Table I.

TABLE I

Incidence of Acute Intestinal Obstruction at the Los Angeles County Hospital, 1941 to 1945.	
Obstruction by Bands and Adhesions.....	359
Early postoperative	31
Late postoperative	274
Without previous surgery	54
Strangulated External Hernia	292
Carcinoma of Colon	105
Sigmoid and Descending Colon	90
Splenic Flexure	9
Transverse	6
Hepatic Flexure	9
Caecum and Ascending Colon	11
Volvulus	72
Large Bowel	27
Small Bowel	45
Carcinoma of Rectum	27
Diverticulitis	24
Intussusception	39
Strangulated Internal Hernia	11
Mesenteric Thrombosis	38
Congenital Anomalies	32
Imperforate anus	13
Congenital atresia	7
Megacolon	4
Meckel's diverticulum	8
Gallstone or Foreign Body	7
Endometriosis	2
Regional Ileitis	4
Extrinsic Tumor	5
Primary Tumor of the Small Bowel	3
Metastases, terminal	51

Obstruction from Superior Mesenteric	
Artery	2
Tuberculosis of Caecum and Peritoneum....	5
Radiation Obstruction	1
Stricture of the Rectum	5
Trauma	3
Total	1,107

TYPES OF OBSTRUCTION:

There are essentially two types of intestinal obstruction, the so-called simple obstruction and the strangulating obstruction.

Simple obstruction is represented by those cases in which there is a blockage of the continuity of the bowel. In strangulating obstruction there is in addition a compromise of the blood supply. Although the definition of both appears simple, the clinical differentiation is by no means as easy. Common examples of obstruction which are always of a strangulating nature are: strangulated external and internal hernias, volvulus and intussusception. Common examples of simple obstruction are those caused by bands and adhesions. In McKittrick's (2) series, 32 per cent of obstructions caused by bands and adhesions were strangulated, and in Dixon's (3) group at the Mayo Clinic 26 per cent were strangulated.

In the simple obstruction, death is caused by gaseous distention, fluid and electrolyte loss, and possible toxic absorption. In strangulating obstruction there is an additional factor of plasma and blood loss, shock, peritonitis and actual necrosis of the bowel itself.

Hartwell (4) has shown that death in simple obstruction of the upper small bowel is due to electrolyte loss which can be controlled by intravenous saline solution.

Wangensteen (5) has demonstrated that the gaseous distention is almost wholly due to swallowed air, and the use of indwelling gastric siphonage is based upon his findings. In simple obstruction the accepted method of treatment is decompression with fluid and electrolyte replacement, whereas early surgical interference is paramount in the strangulating lesion.

As stated, the differential diagnosis between a simple and a strangulating lesion is not easy, and what at first may be a simple obstruction

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may in a short time become a strangulating obstruction, as evidenced by the (25%) band adhesions which are strangulating and the obstruction of the large bowel which soon becomes strangulating because of the closed loop caused by the ileocaecal valve.

The criteria for the diagnosis of intestinal obstruction are fairly clear cut, but the preoperative diagnosis between a simple and a strangulating lesion is often difficult. Wangenstein (6) states that a differential diagnosis can frequently be made by spot tenderness, due to peritoneal irritation present in the strangulating lesion. Dennis and Brown (7) state that pain persisting between cramps, tenderness and rebound tenderness, and shock are characteristics of strangulation. To this Eliason and Welty (8) have added tachycardia and leucocytosis.

At the Los Angeles County Hospital, peritoneal aspiration to determine the presence of bloody fluid has occasionally been used in the past several years; a method also recommended by Hill and O'Laughlin and Stones. (9) By this method a No. 19 spinal needle is inserted into the two lower, and occasionally all four, quadrants of the abdomen. The author has always observed this procedure with apprehension, yet cannot recall of any serious consequences.

Others emphasize the progression of symptoms in spite of supportive therapy. Evans and Bigger (10) have noted a characteristic "position of relief" which the strangulated patient is likely to assume.

In a recent study F. Reinus (11) attempted to point out diagnostic criteria in strangulated obstruction of the small bowel. He classified his patients into three categories: simple obstruction, obstruction with imminent strangulation and obstruction with strangulation. It appeared impossible to point out criteria of imminent strangulation but the following criteria were present in strangulation:

- (1) Steady abdominal pain with sudden onset.
- (2) A seriously ill patient by clinical evaluation.
- (3) Body temperature over 101° .
- (4) Pulse rate over 100.
- (5) The absence of distention in most cases of strangulation.
- (6) Abdominal tenderness.
- (7) A mass on abdominal, rectal or pelvic examination.
- (8) The presence of blood in vomitus or

feces.

Claude Hunt (12) states that Radiography of the abdomen is the most accurate method of diagnosing obstruction and differentiating the type. Simple occlusion with good circulation produces a stepladder pattern of the bowel and allows valvulae connivents to be seen. Strangulation, he states, is shown by lack of a definite pattern. The affected loop is irregularly distended and dark, while valvulae conniventes are invisible or indistinct. Distention, proximal to the loop, begins slowly and is seldom noted early.

In the differential diagnoses there are obviously many factors to be taken into consideration, as briefly outlined on page 28.

In differentiating between simple obstruction, Finney (13) makes this statement: "One rule can be fairly definitely laid down, namely, if colicky pains continue after decompression of the stomach and there has been time for even partial restoration of fluid balance, immediate surgical exploration is necessary."

LARGE BOWEL VERSUS SMALL BOWEL OBSTRUCTION:

The question as to whether an obstruction is in the large or small bowel can frequently be determined by a careful history and physical examination. Obstruction of the rectosigmoid area is the most frequent cause for large bowel obstruction. There the colon is narrower and the lesion, usually carcinoma, is more constricting than the right-sided lesion. Small-bowel obstruction is characterized by early vomiting and late distention with x-ray findings of gas in the small bowel with no gas under tension in the empty colon. In the large-bowel obstruction, distention occurs early, vomiting late, and the large bowel by x-ray is under gaseous tension. In the flat plate x-ray the mistake of interpreting a small bowel under tension as being large bowel is occasionally made. Although large bowel obstruction is primarily a closed loop affair, the ileocaecal valve is incompetent in probably 20 per cent of patients. In these, although obstruction be in the large bowel, gas may also have refluxed into the small bowel. If the least doubt exists, a barium enema should be made.

VOLVULUS:

Patients suffering from a volvulus are likely to have a sudden onset. The patient appears ill from the onset and may be in shock, and

DIAGNOSTIC FEATURES OF SIMPLE AND STRANGULATING OBSTRUCTION.

*Simple***PAIN:**

- | | |
|------------------------|---|
| 1. Insidious or abrupt | 1. Sudden severe most cases |
| 2. Free intervals | 2. Constant with intermittent exacerbations |

VOMITING:

- | | |
|------------|----------------------------|
| 1. Present | 1. Present more frequently |
|------------|----------------------------|

APPEARANCE OF PATIENT:

- | | |
|---|--|
| 1. Early not ill | 1. Ill from start |
| 2. Painful expression only during colic | 2. Constant painful expression more during colic |
| 3. Legs not drawn up | 3. Legs likely drawn up |
| 4. Shock—never | 4. Shock—fairly frequent |

ABDOMINAL FINDINGS:

- | | |
|--|---|
| 1. Distention | 1. Distention |
| 2. Tenderness absent | 2. Tenderness present |
| 3. Rigidity absent | 3. Rigidity sometimes present |
| 4. Mass absent | 4. Mass often present |
| 5. Hernia rings empty | 5. Hernia rings? |
| 6. Ueristaltic sounds metallic or bubbling with peristaltic wave | 6. Peristalsis may be absent or low pitched |

X-RAY

- | | |
|---|---|
| 1. Indicates only obstruction | 1. Indicates only obstruction in most cases |
| 2. Stepladder with valvulae conniventes | 2. Distended loop irregularly distended and dark; valvulae conniventes not distinct |

ABNOMINAL TAP:

- | | |
|-----------------------|--|
| 1. Fluid never bloody | 1. Bloody fluid always indicates strangulation |
|-----------------------|--|

the pain is more or less constant. **Although** when the patient is in shock, pain may not be apparent. There is early tenderness and often rigidity. These patients will often assume a position of lying either on the right or left side, with legs drawn up—the “position of relief” as recently described by Evans and Bigger. (10) The abdomen may early be silent. A spinal needle introduced into the abdominal cavity is frequently a valuable aid. A bloody tinged return from abdominal tap indicates a strangulating lesion. The x-ray usually indicates obstruction but may be of no conclusive aid in differentiating a strangulating lesion, although the criteria mentioned by Hunt, (12) if definite may be of material aid in diagnosis.

Volculus of the large bowel occurs in a 3 to 1 proportion in the sigmoid. The history of previous acute attacks of short duration plus the inability to introduce 500cc. of water by enema has been considered diagnostic in volvulus of the sigmoid by Wangenstein, (6) Barton, Meyer (14) and others, but we have not felt this to be a valuable aid. The history of a fairly sudden onset plus an x-ray picture of a large

sigmoid loop, however, have been diagnostic aids.

INTUSSUSCEPTION:

The diagnosis of intussusception in children, with its frequency of a mass and frequency of a bloody stool and the current jelly on the rectal examining finger, should not be difficult.

HERNIA:

Strangulating internal hernias are rare, and the exact diagnosis is infrequently made before surgery. An x-ray finding, however, of loops of small bowel under tension bunched primarily on one side or the other of the midline should make one suspect paraduodenal hernia. Pain down the inner thigh should make one suspect obturator hernia, particularly if by bimanual examination loops of bowel can be felt in either side of the pelvis.

Diagnosis of strangulating external hernia should be simple, and yet there are patients in whom the hernia is completely missed. This is particularly true in the small femoral hernia. The importance of the necessity of routinely palpating the inguinal and particularly the femoral areas cannot be over emphasized, as local

pain and tenderness will be absent in at least 20 per cent of patients.

Laufman and Daniels (15) have recently reviewed strangulated hernia occurring at Michael Reese and Northwestern University Hospitals. They found that 62 per cent of strangulation occurred in inguinal hernia and 19 per cent each in femoral and umbilical hernia. It is for this reason that the small femoral hernia is not infrequently overlooked.

MANAGEMENT:

The following steps are suggested in the early management of a suspected strangulating obstruction.

1. Do a careful history and physical examination, noting particularly the appearance of the patient. Note just how sick he is. Is the pulse elevated? Is he in constant pain? Are there peristaltic rushes with the pain? Is there early distention? Is there point tenderness between peristaltic waves? Is there a mass? Are the inguinal rings and femoral canals empty? Does a rectal examination reveal a mass or blood?

2. Insert immediate indwelling pastric nasal siphonage. The Miller-Abbott tube is frequently impractical because of the difficulty of introduction beyond the pylorus.

3. Start fluid electrolyte replacement immediately and do urinalysis and obtain blood for count and typing.

4. While the first electrolytefluid replacement is still running, the patient is taken to x-ray for a flat plate of the abdomen preceded by an enema. If in doubt between lower and upper bowel obstruction, a barium enema should be made.

5. If after electrolyte replacement is well going, and if crampy pain persists after the stomach is decompressed, the patient should be taken to surgery immediately and blood and plasma started before the abdomen is opened in all cases.

6. Suction with indwelling tube should be considered an adjuvant in the diagnosis and treatment of intestinal obstruction, and should never be allowed to act as a sedative to the surgeon who may awaken too late to find that he has missed a strangulating intestinal obstruction.

7. In the operative procedure, combating markedly dilated loops of bowel in an attempt to locate the obstructing band is ill advised. The danger from trauma and even laceration

is far greater than the danger of deflation of the gut by a needling or trocar procedure.

8. Closed, so called aseptic, resection have no superiority over open anastomosis, providing the bowel has been aspirated to prevent spillage.

9. In the surgical management of the large bowel obstruction the ordinary caecostomy is inferior to transverse colostomy, as the former does not defunctionalize the bowel and further preoperative preparation of the interval bowel between caecostomy and the causative lesion becomes difficult. Caecostomy, however, has a definite place in those cases where there is a tremendous amount of distention with imminent danger of perforation of the caecum. Gatch, (16) incidentally, makes the statement: "I believe that there is abundant evidence for the belief that the cause of death in obstruction of the large bowel is always perforation of the bowel." When a caecostomy is performed we have preferred the method described by Daniels (17) and a similar one described by Claude Hunt (18) in which their respective, and incidentally very similar, clamps are applied across the exteriorized caecum.

10. Although carcinoma of the sigmoid constitutes the far greater number of obstructions of the sigmoid, one must always be mindful of the possibility of volvulus of the sigmoid. A history of a relatively sudden onset, an x-ray suggesting a large twisted sigmoid loop, and a bloody tinged peritoneal fluid encountered when the abdomen is opened must be considered volvulus until proven otherwise. Needless to say, it is a tragically 100 per cent fatal error to perform a caecostomy or colostomy for volvulus of the sigmoid. Many authors, most recently Hilton and Waugh (19) of the Mayo Clinic, have stated that resection is the method of choice. In those cases we have favored the Mikulicz procedure.

11. In the postoperative management of these patients the antibiotics, fluid and electrolyte replacement are continued, adding potassium on the third day. Blood is given as necessary. Continued suction is carried out until peristalsis is reestablished. With careful management of every detail a lowered mortality should be obtained in intestinal obstruction.

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LARYNGEAL VERTIGO

With Report of Two Cases

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Laryngeal vertigo, known also as laryngeal epilepsy and as tussive syncope (McCann et al, 1949), in which unconsciousness, with or without convulsions, follows vigorous coughing, was first identified as a clinical entity by Charcot in 1876, though Thomas Sydenham in 1679 had remarked upon the vomiting and vertigo which sometimes accompany the severe tussis of grave respiratory disease. The syndrome is perhaps not widely recognized by physicians, but it is probably far from uncommon. Whitty's review in 1943 recorded 85 cases from the literature, and several have since been added. Adams (1936) reported seeing three instances in a period of a few months, and the two patients described in this paper were encountered in successive years, in one of those coincidences which never fail to confound the practitioner.

From the time of the earliest descriptions, the symptom complex has been noted to occur in obese men of middle age, often hypertensive and emphysematous, suffering from chronic laryngitis or bronchitis. Many have been heavy users of tobacco. The cough which precedes the fainting or seizure is most often strong and paroxysmal, but in some reports the cough is specifically stated to have been mild. Proudfit and Karnosh (1949) say that it is distinctive in nature and usually heralded by a tickling sensation in the throat. During an attack the larynx is said to present a picture of glottis and sphincter closure (Jackson and Jackson, 1947). The dis-

turbance of consciousness ranges from mere transient giddiness to a grand mal ictus with prolonged coma.

REPORT OF CASES

Case 1. This somewhat overweight 51 year old white male pensioner was examined at the Veterans Administration Hospital, Tucson, Arizona, on July 11, 1950, on the occasion of a routine check-up. He had been adjudged totally disabled, and his medical condition is adequately attested to by the established diagnoses of arteriosclerotic heart disease with coronary sclerosis, cor pulmonale, and obstructive emphysema. In 1946 he had developed attacks of hard coughing, during which he would lose consciousness, become stiff and twitch. The episodes were irregular in occurrence and rather infrequent; he stated that he had had "about a half-dozen" in the past two years. Three months prior to the time of examination he had suffered from a typical seizure while driving his automobile, as a result of which he had driven off the road and wrecked his vehicle, though he had fortunately not been seriously injured. The patient could recall no aura and did not feel that the cough which preceded syncope was in any way unusual except for its severity. During each period of coma, which evidently lasted some minutes, he had what had been described to him by observers as a fit, and which was obviously a grand mal succession of tonus and clonus. However, he had never experienced incontinence or tongue-biting. Often he would regain consciousness while still clonic, and after an attack he

was sleepy and confused. There was no family history of convulsive disease. The past history was non-contributory. The principal present symptoms which could be ascribed to his cardiovascular disease were dyspnea and undue fatigue. He had no bronchitis or laryngitis.

Psychiatric examination revealed no significant abnormalities except for a retrograde amnesia, which he himself acknowledged. Neurological survey demonstrated no focal disease. The deep reflexes were all very brisk, but there were no pathological responses. The pupils reacted slowly and incompletely to light. The optic discs were flat and the retinal vessels were essentially normal, without any marked arteriosclerotic alterations.

Routine laboratory tests were within physiological limits. An electroencephalogram was performed on July 19, 1950 at the Tucson Medical Center. A monopolar recording with standard electrode placements was made on a Grass eight channel Model III-c electroencephalograph. The tracing showed a basic 10 per second alpha rhythm, interrupted by slow waves at 5-6 per second in runs and by stretches of 25 per second fast activity. No true seizure configurations were seen, and hyperventilation did not materially alter the potentials. There was no focal distribution of either the slow or fast forms. The tracing was interpreted as demonstrating a mild cerebral dysrhythmia, consonant with an interseizure tracing in an epileptic subject.

Case 2*. This obese 67 year old white male was admitted to St. Mary's Hospital, Tucson, Arizona on September 4, 1949. On the preceding day, during a bout of coughing, he had lost consciousness, fallen, and struck the left parietotemporal area of his head on a tile floor. He was unconscious for a few minutes, but there was no convulsion. Attempts to recall events immediately preceding the accident revealed that there was a considerable retrograde amnesic gap. The only other subsequent symptoms were generalized headache and tenderness of the left side of the cranium. Neurologic examination by another physician shortly after the episode disclosed only dubious, minimal elevation of the optic discs, absence of the right biceps reflex, decreased right abdominal skin reflexes, and failure to obtain the quadriceps and triceps su-

rae reflexes. The past history revealed that the patient had for some years had frequent spells of syncope associated with paroxysmal coughing. No description of convulsions could be obtained, either from the patient or his wife or his family physician. There was no family history of epilepsy. The patient was a known diabetic. In the hospital routine blood count was normal except for a white cell count of 12,250, with 68 per cent neutrophils. The urine showed a two plus sugar and a trace of acetone, while the fasting blood sugar was 210 mgms. per cent. Electrocardiogram demonstrated a left axis shift and a tendency toward a low voltage and was interpreted as a borderline tracing. Roentgenograms of the skull revealed a long fine linear fracture originating in the left parietal bone and extending downward and forward through the superior portion of the temporal bone, terminating in the left temporal fossa. Though none of the clinical stigmata of epidural hemorrhage were present at any time, there was no doubt that the fracture crossed the groove of the middle meningeal artery. Chronic maxillary, frontal and ethmoid sinusitis was also evident. Routine physical examination indicated nothing of importance except for musical rales throughout both lung fields. He had been known for years to have a chronic bronchitis with acute exacerbations.

The patient was seen in neuropsychiatric consultation on the 4th hospital day. There were no evidences of intrinsic psychiatric disease. On neurological evaluation the only focal findings were slight increase in the right biceps reflex, decreased right finger-thumb reflex, and a minimal extensor response to plantar stimulation of the right foot. These were felt to be possible results of injury to the left fronto-parietal cortex. It was also noted that the quadriceps and triceps surae reflexes were absent, but this abnormality was ascribed to the long-standing diabetes. The eyegrounds were normal.

The hospital course was uneventful. The bronchitis was symptomatically relieved; the headache disappeared within a few days; and his diabetes was brought under control by diet and insulin. He was discharged symptom-free after 10 hospital days. An electroencephalogram was not obtained.

DISCUSSION

The cause of the unconsciousness which accompanies the coughing of laryngeal vertigo has

*This case is included with the permission and through the courtesy of Drs. Dan L. Mahoney and Robert E. Hastings, both of Tucson.

been a matter of considerable disagreement. Three major explanations have been advanced: that the manifestation is a genuine epilepsy, that it is a reflex phenomenon, and that it is due to cardiovascular changes which produce cerebral anoxia.

Whitty (1943) espouses the theory that the syndrome is true convulsive disease, either a reflex laryngeal epilepsy, epilepsy with a laryngeal aura, or epilepsy consequent to vascular change in a dysrhythmically predisposed cortex. The observation of Proudfit and Karnosh (1949) that there is a peculiar tickling in the throat prior to the onset of the coughing might be adduced as support for this hypothesis. However, there are strong objections to this view as a total explanation. In only one of Whitty's own cases was there an electroencephalogram suggestive of a diagnosis of convulsive illness. Proudfit and Karnosh (1949) point out that a normal brain wave tracing is the rule; all of their subjects had physiological cortical rhythms. Furthermore, most of the patients reported have had simple syncope rather than a convulsion. The belief of Wilson (1931) that laryngeal vertigo is related to cataplexy seems even more untenable. Cataplexy is usually seen as a part of the narcolepsy complex, and no-one has remarked on any concurrence of tussive syncope and narcolepsy. The association of unconsciousness with laughing or excitement in cataplexy would seem to be an entirely different mechanism.

A speculation which deserves more consideration is that which assumes a reflex cause for the unconsciousness. The carotid sinus reflex has been considered as operative but Proudfit and Karnosh (1949) dispose of this possibility by pointing out that cough plays no part in the usual case of carotid sinus syncope and that in no case of laryngeal vertigo tested has the carotid sinus reflex been overly active. More acceptable is the idea of a direct reflex originating in the larynx or the bronchi. Proudfit and Karnosh (1949) give this considerable weight in their discussion. They point out that sensory nerve endings are known to exist in the upper respiratory tract, stimulation of which can cause cardiac inhibition or arrest, or that reflex syncope could be mediated through the aortic or cardiac depressor nerve from stimulation of its receptors in the pulmonary vessels. As ancillary evidence, fainting has been produced in some persons by

motion of the larynx in the simple act of talking (Penfield and McEachern, 1946). On the other hand, no-one has reported reproduction of the syndrome by stimulating the larynx, and there are no accounts of cardiac inhibition during attacks.

The most acceptable theory is that which ascribes the unconsciousness to changes in the cerebral circulation due to intrathoracic pressure and cardiac alterations. It seems likely that in severe coughing the subject unwittingly performs Valsalva's experiment of forced expiration against a closed glottis. In this maneuver the negative intrathoracic pressure is abolished and a positive pressure substituted; with impeded flow into the right auricle the peripheral venous pressure rises, and the veins of the neck and head become distended (Best and Taylor, 1945). Wilkins and Friedland (1944) demonstrated loss of consciousness in performance of the Valsalva experiment, and recorded concomitant diminution in venous return and cardiac output. Rook (1946) favored the principle that cerebral congestion with anoxia and increased intracranial pressure caused the fainting, and more recently in a detailed study of two patients with laryngeal vertigo McCann and his co-workers (1949) have documented this thesis very convincingly, by cardiac catheterization and cine-fluorographic observation during bouts of coughing and during the deliberate performance of the Valsalva maneuver. In one patient syncope and convulsion could be produced, and in both there were extraordinarily high pressures in the right ventricle. In the first there was fluoroscopic evidence of trapping of blood in the pulmonary circulation, as shown by bulging of the right atrium, the venae cavae and the pulmonary conus, and greater density of the hilar root shadows. It was felt that this experiment proved that syncope resulted from cerebral venous congestion, lessened cardiac output, and subsequent anoxemia. They were unable completely to explain the mechanism of the augmented right ventricular pressure and stated that there is perhaps a reflex spasm of the pulmonary artery, in view of the fact that high right ventricular pressures could not be prevented by intubation of the trachea with a bronchoscope. In this connection McCann and his fellow authors (1949) noted the possibility that nicotine from excessive smoking might play a role by affecting the sympathetic ganglia supplying the lungs, since it is

known that the initial application of nicotine to the analogous sympathetic ganglia of dogs causes vasoconstriction. Finally it may be remarked, following Proudfit and Karnosh (1949), that lowering the head of itself effects engorgement of the intracranial vessels and at times subsequent syncope, and that this is just the posture of strenuous coughing.

Even if, as seems likely, the fainting occurring after forceful coughing is due to the intracerebral vascular changes occurring as the result of an increase in intrathoracic pressure, the few cases remain to be explained in which convulsions occur as a complication. Unfortunately electroencephalograms have not been routinely performed. In the first case reported by McCann et al (1949), the EEG was negative, though the patient did have brief clonic seizures. One of the persons discussed by Whitty (1943) and the first patient presented here did have significant cerebral dysrhythmia. It is a supportable thesis that those individuals with tussive syncope who have grand mal attacks during the unconscious period are probably persons with a latent cerebral dysrhythmia. It may be observed that a single negative electroencephalogram means little, since it is well known that an appreciable percent of frank epileptics will show normal tracings. On the other hand, the majority of the cases of tussive syncope, in which no convulsions develop, are probably subjects with electrically normal cortices. In our second patient an electroencephalogram was not obtained, but there is no reason to suspect that it would have been pathological, since his many episodes had never once been epileptic. Anoxia of itself will not produce seizures, but oxygen lack can act as a sufficient trigger for a convulsion, probably by predisposing to a cortical electrical build-up through interference with the competence of the homeostatic mechanisms which control the carbon-dioxide level. (Gibbs and Gibbs, 1950). Recently Kershman (1949) has discussed a group of patients with very rare seizures, one, two, or three in a lifetime. For such individuals he proposes the term "encephalosyncope": Gibbs, Gibbs and Lennox (1937) had previously suggested the term "cerebral dysrhythmia," though the usage "latent epilepsy" has been in more common neurological employment. The general purpose of such euphemisms has been to avoid stigmatizing patients by use of the word "epilepsy," which obviously has a

more serious clinical significance. One of the subgroups described by Kershman (1949) is comprised of persons with a diffuse slow dysrhythmia in the electroencephalogram and a history of rare attacks, precipitated by fatigue or emotional or physical stress. It would seem entirely possible that patients with laryngeal vertigo, who have convulsions in association with coughing but at no other time, might well fall within this group, particularly when they can be shown to have a diffuse dysrhythmia, as was the case with the second man herein described. The grand mal would then be explained on the basis of a pre-existing electrical cortical abnormality of a subclinical variety, raised to the level of epileptic ictus by cerebral vascular changes. Additional proof might be given by testing a number of known epileptics with the Valsalva maneuver, to see if convulsions could be produced. However this experiment would not be conclusive, since epileptics vary in their convulsive responsiveness to various stimuli. In the last analysis it will be necessary to test cases of laryngeal vertigo with serial electroencephalograms to see if the hypothesis is sustained that those having seizures as a part of the symptom picture show a cerebral dysrhythmia, while those with simple syncope possess normal cortical potentials.

SUMMARY AND CONCLUSIONS

Laryngeal vertigo or laryngeal epilepsy is a syndrome in which severe coughing brings about unconsciousness. The probable reason for the fainting is that in coughing the patient performs the Valsalva maneuver of forced expiration against a closed glottis, increasing intrathoracic pressure, causing venous congestion of the head, lowering cardiac output, and bringing about cerebral anoxia. If it were not for the usual conservative adherence to established medical nomenclature, it would be best to advise the term tussive syncope, as suggested by McCann and his co-workers (1949), for the symptoms have nothing to do with the larynx, vertigo is not present, and epilepsy occurs rarely and then only as a complication in predisposed persons. Two cases are here reported as examples of the syndrome with and without convulsions. When grand mal attacks occur during the syncopal episode, it seems likely that the patient has a latent cerebral dysrhythmia. Therapy narrows down to symptomatic treatment of the cause of the cough. In cases with an epileptic com-

ponent, anti-convulsants should presumably be prescribed.

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BASIC SCIENCE SEMINAR

PHARMACOLOGY OF THE ANTIHISTAMINIC DRUGS

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Since ancient times it has been known that certain ordinarily innocuous substances produce in a few people violent disturbances such as skin rashes, hay fever or asthma. Obviously, such disturbances are not entirely due to the exciting agents which are frequently such materials as eggs, oysters, strawberries, pollen inhalations, etc. Undoubtedly there prevails an individual predisposition (the so called allergy) which manifests itself only when the subject comes in contact with the offending substance. The nature of this predisposition and the primary pathogenesis of the disease symptoms became known when attempts were made to immunize dogs against poisonous substances by repeated injections. Instead of the expected preventive or prophylactic action the opposite occurred: a few seconds after a second injection of the substance the dog vomited, developed dyspnea and died within an hour. Post mortem examination showed marked congestion of the liver and intestines. The reversal of prophylaxis was called anaphylaxis.)Richet et al 1898).

All proteins, even non-poisonous ones, may produce anaphylaxis in a variety of animals. The reaction is specific for the protein first injected. When the first (sensitizing) reaction has been made with horse serum the same serum must be reinjected if anaphylaxis is to be obtained. Once established anaphylaxis remains for a long time but can be relieved by repeated small injections of the specific protein. An ani-

mal which survives the anaphylactic shock produced by a second injection, becomes immune to subsequent injections.

Sensitization or anaphylaxis may occur from very small doses; as little as 0.00000005 mgm intravenously or subcutaneously of egg white may sensitize a guinea pig after an interval of 6 to 10 days (incubation period) (Sewall 1914). Maximum sensitization is reached faster with low than with high doses. Injection of serum of a sensitized animal transfers sensitization to the animal receiving the injection; but anaphylaxis is also located in tissues since a sensitized animal cannot be relieved of his anaphylactic response by transfusion with fresh blood. The provocative dose must be larger than the sensitizing one.

These experimental findings, particularly the striking smallness of the sensitizing dose, explains why an anaphylactic or allergic condition is produced in man through the absorption of diminutive amounts of foreign protein by injection (food protein), inhalation (Pollen, various dusts), through trauma and burns (degraded tissue acting as foreign protein) or through infections (bacterial Protein). An anaphylactic state thus produced constitutes a true allergy.

The animal experiments described also point to a method of treatment-desensitization by injection of small doses of the sensitizing substances (Prausnitz-Kuestner). Intracutaneous injections are made at different sites with a large

number of materials of protein nature which are known to produce allergy; the so called antigens. The specific antigen can be recognized by local inflammation (manifested by a wheel which it produces around the site of injection.) This antigen is then repeatedly injected in small doses in order to effect immunization. The method, although cumbersome and difficult to use, is still the method of choice in order to obtain a cure of the allergic state.

The specific antigen determined by the skin test is hardly ever defined with a fair degree of accuracy. Usually it can only be designated according to the source of its origin. Evidently such a poorly defined material must also be of variable composition—which may account for the uncertainty of the results obtained by immunization.

The difficulty of finding the specific antigen is furthermore increased by the fact that the toxic manifestations produced by a multitude of antigens are always quite similar to each other. They resemble histamine poisoning as was first pointed out by Dale and Laidlaw in 1910. Much evidence incriminating histamine as the mediator of anaphylaxis has been collected.

Histamine can be demonstrated as a normal tissue constituent so that there is reasonable evidence for the source of histamine in anaphylaxis (Best et al, 1927). The variation in the anaphylactic manifestations in different species can be explained on the basis of quantitative variations in histamine content. The lungs of guinea pigs and the livers of dogs are reduced in histamine content in anaphylactic shock (K. Watanabe, 1931). A histamine-like substance can be demonstrated in the blood and thoracic duct lymph of the dog during the anaphylactic attack, and in the blood of the guinea pig. The amounts of unbound histamine found in the anaphylactic dog in the blood of the inferior vena cava are similar to those amounts which are required to produce the same vascular changes by intravenous injection (Dragstadt and Meade 1936) whereas in the normal blood of man horse, goat, calf, and guinea pig, 70% to 100% of the histamine present is not free but held in the white blood cells (Code 1937).

All these findings show that histamine constitutes a potent factor in the production of the symptoms of anaphylaxis.

However, not all anaphylactic manifestations can be explained on the basis of histamine action.

One such phenomenon is the incoagulability of the blood. This can be accounted for by the increased production of heparin in anaphylaxis. But other anaphylactic manifestations, not attributable to histamine, are still of obscure origin. Examples are the increased blood coagulability in the beginning, the leukopenia, the changed sedimentation rate and the delayed death from anaphylactic shock occurring in some instances.

Obviously, histamine alone does not account for all symptoms of the anaphylactic shock. Nor is pure histamine invariably the sole causative agent. There may be histamine-like substances sometimes called H-substances.

Concerning the mechanism of the anaphylactic reaction it may be assumed that the sensitizing injection leads to the formation of enzymes which decompose the foreign body protein. Subsequently, when the provocative dose is injected, this enzyme leads to the rapid decomposition of the foreign body protein, whereby histamine in larger than normal amounts is formed.

Nonspecific drugs which partly relieve allergic symptoms in some cases are epinephrine, pituitrin and calcium salts none of which specifically antagonize histamine.

A direct attack on the problem of non-specific allergy treatment was successful only after specific anti-histamine drugs had been found. The modern treatment of allergy is based on the use of such specific compounds. They probably act by means of competitive attachment to cell receptors, thereby displacing histamine from its site of action.

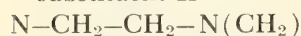
Plain amino acids, notably arginin, were first found to have some such action on the sensitized rabbit gut in vitro, but they proved not sufficiently active and too toxic for practical use (Edlbacher 1937). Compounds effecting competitive substitution more efficiently were discovered by workers in E. Fourneau's noted laboratory in Paris, who synthesized a series of ether-like compounds composed of various substituted phenols linked to amino alcohols. The phenolic ethers proved too toxic. Another line of antihistamine compounds was synthesized in 1912, in France by Mosnier and studied by Halpern in 1942. These drugs were substitution products of ethylene diamine $\text{H}_2\text{N}-\text{CH}_2-\text{CH}_2-\text{N}; (\text{CH}_3)_2$

In this simple compound, two methyl groups are substituted into one of the amino groups.

The other amino group is substituted by more extended groups so that the pattern of all these compounds is

substituent I

substituent II



Out of a large number of such compounds synthesized by Mosnier the least toxic and the most efficient ones were:

- 1) Antergan in which substituent I is a phenyl group C_6H_5

Substituent II is a benzyl group $\text{C}_6\text{H}_5\text{CH}_2$ (B.N.Halpern 1942).

- 2) Neoantergan in which substituent I is a methoxy benzyl group

Substituent II is a pyridyl group (D. Bovet 1944)

After the war this line of research was continued in the United States. Additional ethylene diamine derivatives were synthesized and tested for antihistamine action. The most successful of these compounds is pyribenzamine a dimethyl ethylene diamine in which substituent I is a benzyl group $\text{C}_6\text{H}_5\text{CH}_2$ and substituent II is a pyridyl group. (Mayer, Huttner and Scholz 1945).

This differs from neoantergan merely by the omission of the methoxy group. Nevertheless this slight omission considerably improves the action. Pyribenzamine is the most promising antihistamine agent yet known.

Pyribenzamine is used as the hydrochloride, (synonym diamino benzopyryl Chemically dimethyl-benzyl pyridyl-ethylene diamine hydrochloride), colorless, stable in aqueous solution 1 part dissolves in 0.8 parts of water, pH of solution 6.6 to 6.7.

In experiments on asthma and convulsions produced in guinea pigs by inhalation of histamine, the subcutaneous injection of 0.1 mg/kg of pyribenzamine HCL equally effective as a preventative as 1.0 mg/kg of antergan. Mayer, Huttner and Scholz 1945.

Like other antihistamine agents pyribenzamine is primarily a relaxing drug, the relaxation being specifically active whenever the contraction is produced by histamine. Thus, as little as 0.02 microgram per cc. of pyribenzamine prevents the contraction of the guinea pig intestine elicited by 1.0 microgram per cc. of histamine phosphate. Pyribenzamine is much less active when the contraction is produced by acetylcholine. (R. L. Mayer 42) In the isolated guinea pig lung which

is perfused according to Langedorf, the constricting effect of 50 microgram of histamine is prevented or inhibited by 25-50 micrograms of pyribenzamine. This protection lasts for one hour.

When bronchial tone is measured by the Jackson plethysmograph, 5 to 50 micrograms of histamine produces a constriction of the bronchial muscles in some cases at least. This contraction is entirely prevented by pyribenzamine 1-3mg/kg for as long as four hours or more. 3.5 mg/kg of pyribenzamine is sufficient to protect a dog against anaphylaxis.

The maximal tolerated dose is 20 mg/kg in the guinea pig. Toxic doses produce excitation up to the point of convulsive seizure. (Yonkman e.a. 1945). Pyribenzamine has inhibiting action on histamine salivation in cats; it prevents or inhibits histamine whealing in cats and in rabbits.

In a man pyribenzamine inhibits the whealing from histamine specific antigen been venom, and such drugs as atropine physostigmine or pilocarpine particularly on local application.

The salivary secretion in the cat is sensitive indicator for the action of histamine, as little as 10 micrograms of it injected into the Carotid artery promotes salivation on the same side as measured by a cannula in Wharton's duct. This may be entirely prevented by the antihistaminic drugs.

CLINICAL USES. In acute urticaria, a typical allergic disease, relief is obtained by pyribenzamine in 93% of the acute cases and in 75% of the chronic cases. (Arbesman e. a. 1946) In a series of 37 patients with urticaria and angioneurotic edema 78% obtained satisfactory relief. (Feinberg and Friendlander 1946.)

Pyribenzamine was also effective in the relief of dermographism and urticaria factitia. It relieves the itching of acute and chronic atopic dermatitis in 80% of the cases, also the itching of pruritus ani et vulvae is controlled by it in many instances.

In hay fever pyribenzamine produces improvement in 85% in vasomotor rhinitis in 58% (Arbesman e. a. 1946). Feinberg and Friendlander in 1946 reported 82 cases with 64% success in these cases. Relief was more noticeable in those cases which had received desensitizing treatment. The 1946 ragweed season, during which these tests were made, was unusually

In hay fever McElin and Horton report clinical experience with Benadryl HCL in 100 patients, selected as presenting complaints thought

to be due whole or in part to the release of H substance. These clinicians obtained good to excellent results in 22 of 23 cases of hay fever, 6 to 7 cases of vasomotor rhinitis, 2 cases of Meniere's disease associated with urticaria, 2 of 4 cases of asthma, 2 of 4 cases of histamine cephalgia and 2 cases of urticaria and angioneurotic edema. Further carefully controlled studies in man have been made by these investigators who demonstrated the following physiologic actions of Benadryl HCL.

1. It tends to block the response of gastric hydrochloric to the administration of histamine.

2. It depresses the cutaneous vasodilation action caused by intravenous administration of histamine.

3. Alleviates nasal congestion induced by intravenous administration of histamine.

Benadryl HCL has been particularly effective in relieving symptoms of perennial and seasonal allergic rhinitis. Nasal stuffiness, sneezing, and lacrimation are frequently controlled within one-half hour following a single dose of benadryl and relief may last from six to eight hours. In seasonal allergic rhinitis, especially at the height of the fall pollen counts, larger doses and more frequent administration are necessary. Patients with an associated bronchial asthma may also obtain relief from this condition with Benadryl HCL. Twelve patients who had perennial vasomotor rhinitis were treated with Benadryl; Ten obtained almost complete relief, while two experienced no relief. Marked symptomatic relief was obtained in 4 patients with hyperplastic ethmoiditis. Retraction and disappearance of polypoid tissue occurred and there was diminution of disappearance of purulent discharge. In all cases, however, symptoms returned within 12 hours after discontinuing the drug.

Urticaria, erythema, and pruritis accompanying serum sickness have been relieved by administration of a dose of 100 mg of benadryl every four hours. In some patients, the temperature subsided but joint pains accompanying this condition have not been entirely relieved by this drug. The course of erythema multiforme has been shortened and symptoms alleviated in a number of cases by administration of 50 mg of benadryl every four hours.

The average dose is 50 mg 3 or 4 times daily. In treatment of acute conditions patients should be instructed to await the effect of the first dose for at least 2 hours since partial or complete

symptomatic relief may follow the initial dose. In this event a second dose may not be required for 5 or 6 hours. In severe acute and chronic states as many as 200 to 300 mg daily may be required.

Comparative experiments were done with the following antihistamine drugs; antergan neo-antergan, benadryl and pyribenzamine (Feinberg 1946). Whealing from agents producing urticaria is inhibited by all these drugs to nearly the same extent, but pyribenzamine and neo-antergan seem to be most potent in that respect. Experiments were performed which aimed at finding the minimal dose of histamine fatal to guinea pigs which had been injected with 3 mg/kg of any one of these drugs. The following results were obtained:

- ° 0.4 mg/kg histamine fatal in unprotected guinea pig
- 2.0 mg/kg histamine fatal after benadryl 3 mg
- 2.4 mg/kg histamine fatal after antergan 3 mg
- 15.0 mg/kg histamine fatal after pyribenzamine 3 mg
- 50.0 mg/kg histamine fatal after neo-antergan 3 mg

In therapeutic tests, benadryl and pyribenzamine were compared; these two drugs produced nearly equal results in urticaria, atopic dermatitis and in the edema or eruption from penicillin or sulfa drugs (resembling serum sickness). Either one of the two drugs gave better results occasionally. Benadryl proved superior whenever the additional sedative effect was an advantage as in the relief of itching. On the other hand pyribenzamine gave better results in some cases due to the fact that larger doses of this drug are tolerated. In perennial vasomotor rhinitis benadryl gave relief in 15%, pyribenzamine in 64%. The comparative results in other allergic manifestations of the respiratory tract are listed below.

	Relief from pyribenzamine	Relief from Benadryl
Seasonal hay fever	82%	52%
Allergic rhinitis	48%	13%
Asthma	24%	10%

No cases were observed in which Benadryl was of help after pyribenzamine had failed to bring relief, but vice versa several were improved by pyribenzamine after benadryl had failed. More than half of all patients taking 50 mg or more of benadryl complained of sleepiness or other symptoms; dizziness or lassitude were often so

intense that treatment had to be discontinued. The side effects from pyribenzamine were found to be milder and to occur in less than 25% of the cases, the most common side effect being drowsiness which, however, was much milder than that following benadryl. Rarely was pyribenzamine contraindicated because of side effects.

All of these agents give only temporary relief. They are rapidly absorbed and eliminated within a few hours. A more lasting relief of the symp-

toms can be expected only from immunization. Nevertheless the practical success of benadryl and pyribenzamine has exceeded all expectations. They belong to that small class of drugs for which, immediately after introduction, the demand was so strong that it was impossible to produce enough of the drugs. Undoubtedly a new era in the field of anti-allergic actions has thus been initiated. It seems likely that in the future better antihistaminic drugs will be developed.

ARIZONA MEDICAL PROBLEMS

Consultation and Case-analyses

NOTE—Difficult or unsolved cases are selected from time to time from the practice of Arizona physicians by one of the editors, W. H. Oatway Jr. They are presented to nationally known specialists in the field involved for analysis and opinion.

The *current case* is a serious yet not uncommon problem in internal medicine. It also contains a surgical aspect. The patient had a *jaundice* of indefinite origin, a confusing history, and came to an indeterminate operation.

The *consultant* for the case is Dr. H. MARVIN POLLARD of Ann Arbor, Michigan.

Dr. Pollard is Associate Professor of Medicine in the University of Michigan School of Medicine, a physician in charge of a service at the University Hospital, the associate of Dr. Cyrus C. Sturgis in practice, and an internist who has done considerable clinical research on diseases of the intestinal tract. He has recently published articles on amebiasis, enterogastrone, and other internal medical subjects.

CASE NUMBER XXVI

The patient was a *white male* of 46 years. He came to Arizona from Ohio only two weeks before he was first seen in the office.

His *chief complaint* was a *jaundice* of several days duration, but he had numerous other symptoms and a complicated social and medical history.

The patient's family history was negative, his early medical history included '*spleen trouble*' as a child (with no details, nor any later difficulty), and a freedom from the use of alcohol and from venereal disease. He had had frequent 'colds' all his life.

His *occupation* had been that of a worker

in a steelmill, and he had been a foreman for the past 20 years. He had always worked in the foundry section, with exposure to sand-dust from castings.

Six months before his present illness, in May, he developed a *pain in the lower left chest*, fever and sweats, pain in the epigastrium, some difficulty in urination, and constipation. He was sent to a local Ohio hospital, was said to have 'kidney trouble', had sulfa pills, became worse, and was sent to the Cleveland Clinic. An examination of the urinary tract showed it to be normal, but no other diagnosis was made.

He continued to lose weight (from 138 to 110 pounds) and his fever persisted. His hometown doctor found a density in the left chest, sent him to a hospital, and 1½ *quarts of fluid* were aspirated. The fever and pain disappeared and he gained weight.

Three weeks later the *pain in his back and epigastrium* returned, and he went to the Mayo Clinic. They found his kidneys normal, his blood count and sedimentation rate normal, noted the subsiding effusion and a generalized pulmonary nodulation which was considered to be questionably miliary tuberculosis, and advised against an exploratory for the cause of the epigastric pain. They wondered whether it might be a pancreatic lesion.

After resting at home for a time the family came to Arizona to avoid the respiratory infections to which the patient was subject.

Jaundice developed within 2 weeks, and he noted that his urine was a dark brown. The pain in the back persisted, and was 'in the small of his back', medially. By systems he had noted frontal headaches, recent vertigo and double vision, nervousness, insomnia, occasional recent nosebleeds, dry mouth, anorexia, indigestion

from meats, a slight burning pain in the abdomen relieved by liquids, constipation since jaundice, normal colored stools, and a slight but tender swelling of the right hand and knee. Edema of the ankles had been present last year, but absent since. There were no important urinary symptoms.

By physical examination he was seen to be tired and thin, tho his weight was only 5 pounds less than average. There was a moderate jaundice of the skin and sclerae, and a folliculitis of the back. His tongue was pallid and coated, the pulse was 90, BP 112/80, the temperature was 99.4 degrees, and the prostate was normal.

There was a flat tender area in the lower dorsal spine. The abdomen was flat, slightly tympanitic, and very tender in the right subcostal area. The liver was enlarged to 4 cm. below the costal margin, but the spleen was not enlarged.

Fluoroscopy showed the same changes which were present in a film which had been taken 6 months earlier,—a normal heart and aorta; a calcified Ghon tubercle in the left hilus, a minimal scarred patch in the right apex, and no evidence of pleural disease.

The blood count showed a normal RBC and hemoglobin; a WBC of 6,400, with 69% neutrophils. The urine contained a trace of albumin, one plus sugar, a strongly positive bile test, and urobilinogen in 1:30 dilution. The Van den Bergh direct was 4 plus, and the indirect equalled 10 mg. No blood serum amylase was obtained.

A partial gastro-intestinal series showed a normal stomach and duodenum, with no evidence of a mass in the pancreatic area.

The original impression had not yet crystallized when two days later his stools became a yellowish-white and his temperature rose to 102 degrees. The stools and symptoms remained the same for a week, tho the fever subsided. He refused hospitalization until the twelfth day, when his stools became less pigmented, he lost appetite and weight, and he became mildly stuporous. His temperature went to 101 degrees and was remittent. The abdominal and spinal pain remained steady and non-colicky, and seemed to be referred to the back.

He was seen by a surgeon in consultation in the hospital and it was agreed that the condition was an obstruction of the common bile duct, either by stone or a pancreatic tumor. An

exploratory laparotomy was recommended and accepted.

Surgery was performed 2 weeks after he was first seen, and 2½ weeks after the onset of his jaundice. The abdomen contained a large amount of bile-stained serum; the gall bladder was greatly enlarged and tense; the pancreas was enlarged to three times normal size but contained no tumor; the gall-bladder, cystic duct, and common duct were free of stones, but a probe could not be passed thru the common duct due to a "bowel obstruction a short distance below the cystic duct". A cholecystostomy was performed and the incision closed.

The post-operative condition was fair. The jaundice remained deep in spite of a drainage of 1,000 to 1,600 cc. per day. Supportive diet, fluids, and vitamins were used, but his general condition deteriorated. The fever subsided on the second day, but he was often delirious, the renal function was poor, and he died on the tenth P. O. day. A necropsy was not allowed. QUESTIONS:—

1. What was the probable diagnosis in this case?
2. How does the diagnosis fit in with his past history?
3. What tests could have been done to make a diagnosis more certain?
4. How could the situation have been managed to change the course of illness?

CASE ANALYSIS

In answer to the probable diagnosis in this case, I should first like to stress a few points in differentiation. The patient's age places him in a vulnerable period for both benign, as well as malignant disease, without favoring either to any great extent. The fact that he saw a physician due to his "jaundice" leads us directly to some process affecting the biliary system, a very obvious, yet an important point. His story of "spleen trouble" as a child, I feel, is more misleading than helpful and I am inclined to discount it. The fact that he has never consumed alcohol has its significance when the individual is faced with a possible diagnosis of cirrhosis of the liver. The occupational history cannot be passed by lightly and one is forced to keep in mind silicosis with its subsequent association with tuberculosis.

Going on to the more acute phase of this patient's illness, he developed pain in the lower

left chest, fever and sweats, as well as pain in the epigastrium six months previously. His initial examination did not, I believe, reveal anything significant associated with the final diagnosis. The administration of sulfa pills could have caused a hepatitis, but I doubt that it did.

The density in the left chest, plus the pleural effusion of one and one-half quarts of fluid, which when removed appeared to have some association with improvement of the fever and relief of pain, seems too simple for a diagnosis of tuberculosis to be made and I believe that it is more likely indicative of a *pulmonary infarction with effusion*, the infarct slowly clearing.

The persistence of the *pain in the back and epigastrium* carries a great deal of significance with reference to the primary disease. I believe that the "generalized pulmonary nodulation," even if it had the appearance of miliary tuberculosis, was more *probably silicosis*, in view of his occupation; I assume that pulmonary metastasis was also considered, and that this prevented his physician from performing a laparotomy at that time. All of his difficulties had not produced *jaundice* until two weeks before the history was taken. The dark urine is merely a manifestation of bile in the urine and favors an *obstructive process* affecting the biliary system. The headaches, vertigo, nervousness, insomnia, nosebleeds, and so forth, are all secondary manifestations of the patient's *bilirubinemia*, I believe. The part which is confusing is the "normally colored stools", and I believe that on closer questioning these would have been found to be light or clay colored. Another confusing feature is the slight, but tender swelling of the right hand and knee, but the *ankle edema* could be explained by liver damage and reduced total serum proteins, or thrombophlebitis.

The evident jaundice on physical examination is significant. The absence of lymph nodes and a palpable spleen lead us away from a diagnosis of lymphoblastoma. The tender area in the lower dorsal spine is confusing. Apparently there was no ascites, but the liver was enlarged and there was tenderness in the right upper quadrant.

The interpretation of the chest fluoroscopy does not indicate the nodularity seen in the chest film six months previously and, hence,

suggests that the nodularity had cleared during this interval of time, or could not be easily visualized.

The bile in the urine, borderline urobilinogen, and four-plus direct Van den Bergh is suggestive of *obstructive jaundice*. The absence of any evidence of a mass in the pancreatic area by x-ray is not surprising and should not deter one from this impression. That the increasing severity of the symptoms, the clay colored stools, and abdominal pain, should lead to surgery is not surprising. *The findings at operation are understandable* with the exception of the actual location of the bowel obstruction, which is not too clearly stated.

I believe that *the significant findings leading to the diagnosis can be summarized as follows*: A six-month history in a forty-six-year-old male, consisting of almost persistent upper abdominal pain with radiation to the back, fever, weight loss, eventual jaundice of an obstructive nature, negative upper gastrointestinal x-ray, relatively normal blood count, enlarged gallbladder and pancreas at operation with a process obstructing the bowel, represents:

1. Carcinoma of the "biliary tree," with secondary pancreatitis.
2. Previous pulmonary infarct, left.
3. Pneumonoconiosis.
4. Thrombophlebitis.

There are very few tests which could have been done to make the diagnosis more certain. The patient should have had sputum examinations early in the disease, in the search for acid-fast bacilli. A tuberculin test would probably have been positive. The pleural fluid should have been cultured for acid, fast bacilli, and studied for malignant cells. Additional liver function studies *might* have assisted in making the differentiation.

Laparotomy, I believe, was imperative and had the patient permitted, should have been done at an earlier date. Even then, the course of his illness would not have been altered appreciably.



PHOENIX CLINICAL CLUB MASSACHUSETTS GENERAL HOSPITAL

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

First Admission: A forty-six year old housewife entered the hospital because of a persistent cough.

Approximately eight months before admission the patient developed a hacking cough and began to raise a small amount of sputum each morning that occasionally was blood tinged. There was slight dyspnea on exertion, but no cyanosis, palpitation, orthopnea, ankle edema, chest pain, fever, chills or night sweats, and she had gained 17 pounds during the six months preceding entry.

The family and past histories were noncontributory. There had been no contact with an open case of tuberculosis. A hysterectomy had been performed nine years before admission.

Physical examination revealed a well-developed obese, apprehensive woman who had a bothersome cough. The heart, lungs and abdomen were normal. A vaginal examination was essentially negative, and the fundus could not be felt.

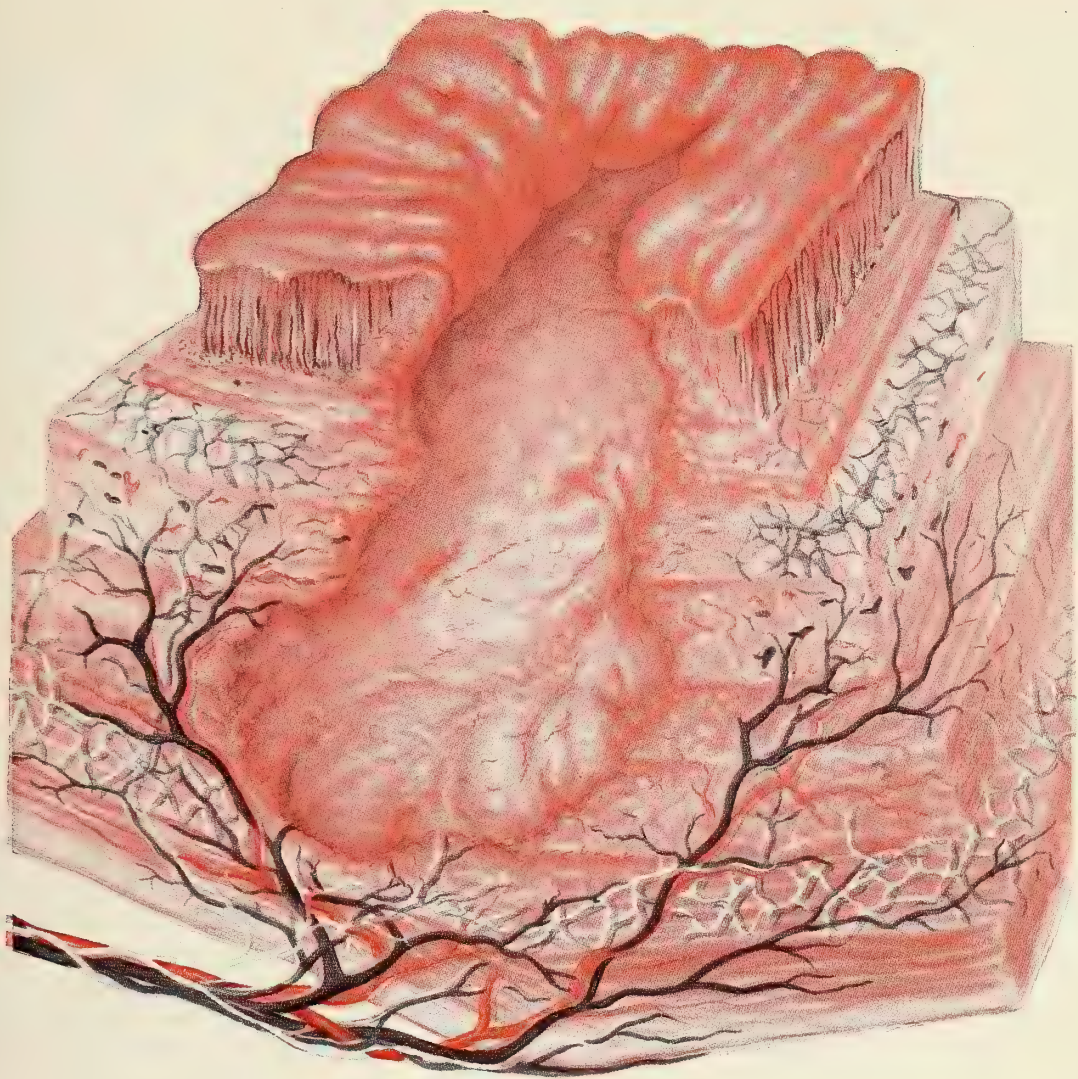
The blood pressure was 130 systolic, 90 diastolic. The temperature was 98.6°F., the pulse 89, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,490,000, with a hemoglobin of 13.6 gm., and a white-cell count of 11,000, with 65 per cent neutrophils, 21 per cent lymphocytes, 10 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. The urine was acid in reaction and had a specific gravity of 1.012, and the sediment contained a rare red and white cell and 3 epithelial cells per high-power field. The blood Hinton test was negative. The sedimentation rate was 2.5 and 9 mm. after thirty, forty-five and 60 minutes respectively. No acid-fast bacilli were seen in seven sputum examinations.

A chest roentgenogram disclosed a rounded, 4 cm., homogeneous area of increased density in the medial portion of the right infraclavicular area, there was no evidence of calcification or of cavity formation and the right lung field was otherwise clear. Overlying the anterior end of the fourth left rib were two irregular areas of increased density. The remainder of the left lung field was clear. The heart and mediastinum were not remarkable, and there was no evidence of respiratory shift. Both sides of the diaphragm were smooth in outline and showed normal motion. A review of films taken prior to entry showed much the same appearance except that the nodules in the left lung field were seen more clearly and appeared to be round rather than irregular. In the flat plate of the abdomen, the kidneys appeared normal in size, shape and position; no stones were seen. Intravenous dye was promptly excreted and outlined normal urinary passages.

Bronchoscopy on the second hospital day disclosed a normal trachea. The left bronchus was not entered, but on entering the right bronchus, the floor was displaced forward by extrinsic pressure. The orifice of the upper-lobe bronchus appeared angulated as though there were outside pressure on the superior angle where this bronchus met the main stem, thus displacing the opening downward and causing the superior lip to present sharply in the main-stem lumen. There was no visible growth, and nothing from which a biopsy could be taken. Sputum was obtained for acid-fast examination. The next day a pneumothorax was started in preparation for thoracoscopy. The patient was discharged unimproved on the ninth hospital day. X-ray films of the chest taken before the pneumothorax yielded no additional findings.

Second admission: (one year later). The patient was readmitted for exploratory thoracostomy. Her symptoms had continued unchanged. An X-ray film of the chest taken a month after discharge revealed that the right lower lung had re-expanded, but that there was still a considerable quantity of air surrounding the collapsed right upper lobe. The mass in the right upper lobe had not changed except that it contained a questionably small area of diminished density suggestive of beginning cavity formation. The nodules in the left mid-lung field were not clearly visible and were approximately 1 cm. in diameter.



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SEARLE RESEARCH IN THE SERVICE OF MEDICINE

WHEN WRITING ADVERTISERS PLEASE MENTION THIS JOURNAL

Physical examination was unchanged. The temperature, pulse and respiration were normal.

An X-ray film of the chest taken on the day of admission revealed that the "mass" in the right upper lobe had increased slightly. There was an area of atelectasis in the anterior portion of the base of the right upper lobe. The two small areas in the left lung field had not changed.

An operation was performed on the seventh hospital day.

DR. HOWELL RANDOLPH:

This 46 year old housewife presented herself with a history of cough for eight months, with a small amount of sputum which was occasionally blood tinged.

Seven examinations of the sputum were negative and all other findings, both laboratory and clinical, were essentially negative except for the X-ray which showed a rounded mass four cm. in diameter in the medial portion of the right infraclavicular area.

Bronchoscopic examination was informative, although no intrabronchial lesion was seen. The right showed "on entering the bronchus that the floor was displaced forward by extrinsic pressure. The orifice of the upper lobe bronchus appeared angulated as though there was outside pressure on the superior angle where this bronchus met the main stem causing the superior lip to be displaced downward and presenting sharply in the main stem lumen. Sputum was obtained for acid fast examination." The results of this examination were not given, but from the management of the case subsequently, it seems that she was not diagnosed to have tuberculosis. Although pneumothorax was given, it was not maintained and was said to be given for diagnostic purposes.

No significant data was submitted for one year when she came in with a mass 7 x 7 x 6 cm. and more evidence of cavitation. There was also an area of atelectasis in the anterior portion of the base of the right upper lobe. The two small areas in the left lung had remained unchanged.

The various fungus infections may, I believe, be ruled out as most unlikely of the possibilities. This would not be true if the patient lived in an area where coccidioidomycosis was common, as this is exactly the picture we have seen in several of these infections.

Tuberculosis would be in the running but un-

likely in view of the many studies that were made in the presence of a cavitary lesion.

Of the malignancies, as carcinoma, the fact that this large rounded mass had increased in size is suggestive, as is the ability to produce pressure upon mediastinal structures. Metastatic carcinoma is not likely if the nodules in the left lung are due to the same cause, as these failed to grow in a year. No primary focus is noted in the examination, but hysterectomy was performed nine years before. The absence of pain in the symptom list in the presence of growing lesion that has produced atelectasis is probably an oversight of the historian. Even tuberculosis will produce pain when atelectasis of a lobule occurs.

Of the benign conditions which might produce this situation, there is the hamartoma of the lung which is rare condition and may be ruled out because it is solid and does not communicate with open bronchus. The various cystic conditions do not seem very likely, even our old friend the echinococcus cyst.

The adenoma of the bronchus is almost always seen in the larger bronchi. They usually occur in women; they are of gradual development, may be very slow growing and may not produce symptoms until bronchial obstruction is produced. They are both benign and malignant, depending upon the pathologist, and a few of them have been proven to produce distant metastases. Moersch in 1945 stated that they were always in the larger bronchi, as did Foster-Carter in a 1941 review of such cases.

In 1947 Herbert Maier reported five cases occurring in branch bronchi not accessible to the bronchoscope. In four of the cases the tumor was located near the hilus area, and in one out in the periphery. Three were asymptomatic and one had bleeding, one pain. All were well three years or more after lobectomy. In none of these was cavitation noted.

There was a recent report of an alveolar cell carcinoma, which may well have been confused with adenoma, inasmuch as it was localized rounded tumor mass on the X-ray. Alveolar cell carcinoma has been recently reported as being a diffuse and slowly progressive condition. The appearance of the lung was compared to that of the sheep dying of Zjakeits epidemic disease and the patient had been in contact with sheep.

So now after surveying the field I am going

to settle for an *adenocarcinoma*, probably bronchogenic.

DR. LESLIE KOBER:

We have here the problem of determining the etiology of this "mass" in the right upper lobe approximately 7 x 7 x 6 cms. with cavity. The present emphasis on cancer of the lung and its early diagnosis would lead one to think immediately that this lesion might be due to bronchogenic carcinoma. Why wasn't an exploratory operation done on the first visit to the hospital one year previously? Even at that time the 8 months old cough with hemoptysis, absence of symptoms, or bacteriological evidence of tuberculosis would certainly have been sufficient to warrant exploratory thoracotomy. We must assume either that the patient refused the operation or that this case occurred before the present era of successful lung surgery. We are told that "a pneumothorax was started in preparation for thoracoscopy", but no information is given as to whether this procedure was completed. Maybe something was found which persuaded them to go no further. At least the patient was discharged shortly thereafter, only to reappear one year later. This immediately brings up the problem of whether bronchogenic carcinoma would have remained so benign for a period of approximately 18 months from the onset of cough.

In a Clinical Club discussion on October 2, 1950, reprinted in *Arizona Medicine* in March, 1951, Baldwin quotes: "According to Rubin three types of bronchogenic carcinoma are recognized: 1) An epidermoid carcinoma, 2) an adenocarcinoma, and 3) an anaplastic type, variously referred to as a small, spindle or round cell carcinoma."

Tenzel noted, as have several others, that epidermoid carcinoma is found chiefly in males, while adenocarcinoma is more frequent in females. Some pathologists have correlated the degree of malignancy of bronchogenic carcinoma with the cellularity of the tumor on the theory that the more cellular the structure, the more malignant and, possibly, the greater its radio sensitivity.

Epidermoid carcinoma is a relatively slow growing, late metastasizing tumor. It is not rare to find at autopsy instances of this type tumor limited to the affected lung and regional lymph nodes without any evidence of tumor elsewhere in the body. Acute cough may pre-

cede more acute symptoms by many months, and again, according to Rubin, may require years. However, 60% of the cases are of less than a year duration, and 30% less than six months. It seems entirely possible then that our case may well be a bronchogenic carcinoma showing cavity formation indicative of central necrosis and abscess formation, as far as duration of lesion is concerned.

The X-ray characteristics distinguishing carcinomatosis from other lung abscesses are:

1. greater thickening, often scalloping of the wall;
2. absence of noteworthy inflammatory changes around the cavity
3. signs of atelectasis and intrathoracic displacements caused by bronchial obstruction; and
4. a lack of change in comparative films.

In the final analysis, however, the diagnosis depends on careful weighing of all the findings. Apparently, seven sputum examinations, absence of fever, normal sedimentation rate, bronchoscopic examination, and X-ray findings had ruled out an active tuberculous lesion one year previously. But at that time it was noted that former round nodules in the left chest had become irregular areas of increased density. One year later these two lesions were unchanged. Are these two lesions identical with the process in the right upper lung? Could all three of these lesions have been inactive tuberculous lesions one year ago and now the right lung lesion become active, developed central necrosis and vacity? It seems that exploratory operation was needed to decide the issue.

Quoting from Frissell, also in *Arizona Medicine* for March, 1951, "I am inclined to go along with Rubin, Judd and other investigators who feel that in obscure lung lesions occurring in elderly individuals, a diagnosis of cancer of the lung is present until definitely proved otherwise." He goes on to quote from Rubin: "Several factors are concerned in apparent increase in incidence of this disease: 1). an aging population, 2). improved methods of diagnosis, particularly bronchoscopic surveys, biopsies, laboratory smear technique, etc. 3). Recent work on inhalation irritants including tobacco smoke. He goes on to quote, "The age incidence of carcinoma of the lung is 40 to 60. Males outrank females 3 to 1. The origin is usually in a major bronchus in 75% of cases. Periphery of

the lung is involved in only 25%. The upper lung field is involved in most instances. Complications include atelectasis, emphysema, and abscess formations in about 35% of the cases, etc. (for further details see the March, 1951 Arizona Medicine.)

Moore also discussed this Clinical Club case of October 2, 1950—presented by Dr. Williams, and ruled out the various causes of lung abscess including tuberculosis, until he arrived at the final conclusion—to quote from Arizona Medicine: "From recent literature the following brief, rather dogmatic statements with reference to cancer of the lung have been gleaned:

1. Bronchogenic carcinoma may simulate any disease, but none more successfully than tuberculosis.
2. The symptoms, physical signs and clinical course are not characteristic, and do not assist in the diagnosis of early bronchogenic carcinoma.
3. The X-ray appearance may resemble (a) benign tumors, (b) tuberculosis, (c) filled cysts, (d) chronic abscess, (e) localized bronchiectasis.
4. The only hope for a cure is by surgery in the stage before the above symptoms, physical findings and clinical course becomes suggestive of the condition.
5. Diagnosis of early bronchogenic carcinoma depends upon the presumptive X-ray findings.
6. It is wise to consider abnormal lung shadows in men over 40 years of age as caused by cancer until proven otherwise.
7. Exploratory thoracotomy when in doubt is the safest course. Palliative treatment, rest cures, and watchful waiting result in deceptive responses and greatly lower the chances of successful treatment.
8. Mass surveys, even by miniature X-rays, will increase the incidence of early detection and enhance the chances for successful treatment."

I quote from the above men, because I feel sure they have all given us the best information available at this time. Furthermore, they all made the diagnosis of Bronchiogenic carcinoma and all were correct—which proves what a wonderful, kind judge can do for ones' ego. Certainly Dr. Balk wouldn't want to let Dr. Williams get ahead of him in the esteem of his fellow practitioners, and no one likes to be

called a lot of low down names. So I'm sure that our kind, gracious, scientifically minded judge today, not knowing that another had previously selected a similar case, chose this case for the specific purpose of once again calling to our attention the facts I have liberally quoted—about the why and wherefores of *cancer of the lung*.

My Diagnosis—Carcinoma of the lung. Probably epidermoid type because of its slow growth, but because adenocarcinoma is more frequently in females we cannot be too specific until the microscopic sections are viewed.

DIFFERENTIAL DIAGNOSIS

Dr. Helen Pittman: I assume that the operation done nine years ago was at an outside hospital; hence we do not know about the ovaries or why the operation was done.

The laboratory findings were essentially normal. It is not stated whether sputum taken at bronchoscopy was examined for tubercle bacilli or what the report was and I do not know why they went ahead and did a thoracoscopy.

This patient was a forty-six-year-old woman in good health. Before the time of operation, she had had, for one year and eight months, a cough productive of small amounts of sputum, which was only occasionally, not regularly or daily, blood tinged. She had had slight dyspnea on exertion, had gained weight and had had a hysterectomy nine years before, for what reason or what was removed we do not know. It is the kind of problem that we are faced with frequently and it is a difficult one because we do not have much to go on. With each case of chest tumor we have to go through rather stereotyped processes of reasoning. First of all, we think of the possible diagnoses and the appropriate diagnostic procedures. If that does not give the answer we must come to the decision whether or not exploration should be done.

The most probable diagnosis is malignant tumor, either primary or secondary. If primary, we think first of primary carcinoma of the bronchus. There was some blood, but it was only occasional, and we have learned to realize that the bleeding which leads us to suspect carcinoma of the bronchus is the daily ooze, not the occasional blood streak. (This patient had pressure on a bronchus that was enough to give an irritating cough and I think we can say that this small amount of bleeding was probably secondary to the irritation that comes from pres-

sure and was not caused by bronchial ulceration. Other primary malignant tumors are extremely rare; these include sarcoma, lymphoma, dermoid cyst and teratoma.

May we see the x-ray films?

Dr. George W. Holmes: The first two films were taken before coming to this hospital. The lesion itself is distinctly lobulated. It varies somewhat in density, and within its substance are bright areas, which I think are bronchi but may be cavities. The heart and mediastinum are not displaced. There are no eroded ribs. The process is not adherent to the pleura because it was easily displaced after giving the pneumothorax. It is in the midchest—neither in front nor in back, nor in the upper or the lower portion. In the opposite lung field there is a small irregular shadow that is visible in most of the plates and does not change appreciably in size during this period of time.

Certainly the change in the size of the lesion itself was not rapid. One must also consider the possibility that a bronchus was plugged and that this shadow was due to atelectatic lung around a mass rather than to the actual mass. There was no fluid in the pleural space.

Dr. Pittman: This does not look to me like metastatic disease in the chest, but we have to think of that and it is quite obvious that they were thinking of it when the patient was worked up on the first admission. There were two possible sources: the unknown pelvic situation nine years before, and the commoner one, hypernephroma which they obviously were considering. This to me is not at all the picture of what one usually sees with metastases from a hypernephroma. But when the flat plate and the pyelograms were made they probably had that in mind, and certainly it was the proper thing to do.

The next thing to consider in a chest of this sort is chronic infection, and the two infections that we see most commonly are tuberculosis and lung abscess. The history does not suggest infection. The patient had gained weight, had no fever, and had no anemia or leukocytosis—the white-cell count of 11,000 with 65 per cent neutrophils is essentially normal. She also had a low normal sedimentation rate. Repeated sputum examinations were negative for tubercle bacilli. We do not know whether acid-fast stains were done on material obtained through the bronchoscope. This is one of the cases in which tests with a series of dilutions of tuber-

culin might have been extremely important. In the presence of this lesion a negative test with a 1:1000 dilution of tuberculin would have enabled one to have ruled out tuberculosis.

Going back to the primary bronchial tumors, I must say that the sputum does not suggest such a tumor or ulceration into the bronchus, and the bronchoscopic examination was negative for a lesion of the bronchial wall. It did, however, show extrinsic pressure, so I think we can fairly safely reject from our minds a primary carcinoma of the bronchus.

Then one must consider benign tumors. This was an essentially asymptomatic mass, which did not affect the patient's health, and on bronchoscopic examination only revealed evidence of extrinsic pressure. Intrathoracic goiter and dermoid cyst are possibilities, but I feel perfectly sure that both can be discarded at this time.

On the patient's first admission she was put through the routine diagnostic procedures of x-ray study, blood work, bronchoscopy and pneumothorax. The last was done to learn whether it caused the lung to fall away from the pleura and hence made the lesion more clearly visible, and at the same time to show up the parietal pleural surface to see if it was rough or showed nodules. At the time of discharge on the first admission the more serious diseases, for which one should interfere, had been ruled out, and given a patient who was not sick it was reasonable to keep her under observation—to let her go home and to see how things went along.

That is apparently what was done. The x-ray taken one month after discharge shows that for at least a month she kept in contact; then she came back the year after the first admission still, we gather, in good health, with no significant change in the symptoms and with no fever. There are no reports of blood, urine and sputum examinations at that time, but I assume that they were still negative. Then comes the situation that must be frequently faced with these tumors. All the routine and reasonable diagnostic procedures have been carried out; the patient is in good health, but there is an increasing lesion. Is one justified in allowing it to ride any longer or must one explore and find out what is at the base of it? I think that is the really important point in this case. One can guess all day long about the diagnosis. All leads have been quite valueless, and while there is still time to do something, one should resort

to exploration for the purpose of diagnosis. I think that was probably the situation in this case.

One should have a preoperative diagnosis for a working basis. There are few clues to throw weight on any of the things that I have discussed. There is little evidence for infection, and a good deal of evidence against it. I am going to make a preoperative diagnosis of tuberculosis; possible the mass was a tuberculoma or a large tubercle.

Dr. Tracy B. Mallory: The preoperative diagnosis was tuberculoma, Dr. Pittman.

Dr. Richard Sweet: This was one of the most amazing cases we have had in a long time and I welcome the opportunity to find out what the pathologists found, because I have not heard. Because of the exigencies of the war, the patient had a complete change of doctors during a period of one and a half years. The surgeon who first saw her went to war, then the medical man went; finally the one who did the bronchoscopy entered the armed services. It was my impression that we did another bronchoscopy at the time of the second admission, but perhaps not. At any rate, the case was presented to me by her new physician for a decision whether we should do, as Dr. Pittman has said, an exploratory operation.

I was impressed by a number of clinical facts regarding this patient. First of all, after a year and a half she was in remarkably good condition and had no fever. This seemed to indicate that she did not have a wasting disease. From that standpoint, as you recall, Doctor Holmes mentioned a lesion in the left lung field, and it is my impression that the surgeon who first reviewed her case believed that because of this lesion and the probability that she had tuberculosis it would be unwise to operate for fear of a flare-up on the left side. Since that time more lobectomies have been done for tuberculosis and perhaps we had more courage at the second admission than we had at the first. I was never convinced of the diagnoses of tuberculosis, although Doctor Mallory has said that the preoperative diagnosis was tuberculosis. My diagnosis was tuberculosis or cancer. I did not see how one could tell which it was. The reason I leaned a little toward cancer was that she had a persistently bloody sputum. It is unfortunate that Doctor Pittman was not given that information in the record. The patient was

worried about herself because of this blood-tinged sputum almost every day. That to me usually means carcinoma. On the other hand the history was a long one. Patients with carcinoma of the lung, even of only a few months' duration, are usually in poor physical condition, but this woman was in good shape. So although we really had no accurate information concerning the diagnosis, I leaned toward carcinoma, as did the medical man who had her in charge, as well as some of the others who saw her, including one physician whose knowledge of tuberculosis is extensive.

At operation the condition was still puzzling. The lesion involved the upper lobe. It was not adherent. As soon as air was introduced into the chest it fell away from the chest wall. It had a round contour like that of a swollen liver. The surface was depressed, and there was a milky film over its surface. As I felt of it, it had a rubbery consistency; it was not hard and firm like a carcinoma. I could not tell what it was. There were no enlarged lymph nodes at the hilum, which is consistent with the diagnosis of tuberculosis. In the majority of carcinoma cases, on the other hand, the nodes are involved. Removal of the lobe was easy. Her convalescence was as smooth and uneventful as any I have ever seen, and that to me is circumstantial evidence in favor of the diagnosis of carcinoma.

Dr. Mallory: Do you care to say any more, Doctor Pittman?

Dr. Pittman: I should feel, as Doctor Sweet did, that if the patient was having daily bleeding one would have to consider carcinoma much more seriously than I considered it, although it certainly is unusual to have a bronchoscopy merely showing evidence of extrinsic pressure.

Dr. Sweet: I do not understand the bronchoscopic report. They say there was evidence of pressure on the trachea or bronchi, but at the time of operation there was none whatever.

Dr. Mallory: Doctor Robbins, have you any comments?

Dr. Lawrence Robbins: No; my diagnosis was tuberculoma from the way the lesion had progressed.

Dr. Holmes: The x-ray evidence is in favor of tuberculoma.

CLINICAL DIAGNOSIS

Carcinoma of lung?

Tuberculoma?

DR. PITTMAN'S DIAGNOSIS

Tuberculoma

ANATOMICAL DIAGNOSIS

Metastatic papillary cystadenocarcinoma of ovary.

PATHOLOGICAL DISCUSSION

Dr. Mallory: Doctor Castelman, who schedules these conferences, sometimes plays a trick on me. When we have a particularly difficult specimen over which I delay about committing myself, he occasionally puts it on for clinicopathological conference without warning and I have to make up my mind. I think that is the reason this case was scheduled.

I am not a bit sure what the diagnosis is. About four fifths of the right upper lobe was replaced by a rather firm, but not extremely hard, tumor. Grossly it looked like tumor and certainly was not tuberculosis, but it was peculiar in several respects. There were four small cystic cavities within the solid tumor that did not seem to be bronchi, and each of them contained mucoid material. They seemed to be part of the tumor.

The microscopic sections present a very unusual appearance. The architecture of the lung is perfectly preserved. The bronchi are lined with perfectly normal ciliated epithelium, and the great majority of the alveoli are lined with extremely high columnar epithelium that is obviously secreting mucus. This epithelium projects into the lumens of the alveoli in papillary masses, and there is no destruction of the alveolar walls that can be clearly outlined by elastic-tissue stains. The appearance of the cells, the papillary character and the mucoid secretion are all similar to the findings in papillary adenocarcinoma of the ovary. This woman had had a hysterectomy nine years previously and we have not yet succeeded in checking up on the findings of that operation. It is conceivable that this represents metastasis from an ovarian tumor. On the other hand this would be an extraordinary course for a malignant ovarian cyst. They almost always extend first through the wall of the cyst to the peritoneum, then produce widespread peritoneal implantations followed by ascites, and distant metastases are quite uncommon. Metastasis from a papillary pseudomucinous ovarian cyst must remain a possibility. It is still a question whether the masses in the other lungs were likewise metastatic, and it is difficult to

explain why one should grow and two others remain the same size.

The other possibility is that this was a primary tumor of the lung, and in favor of that I have seen just one other case which to my recollection is exactly similar in growth and histologic appearance. That case occurred in a man so that ovarian cyst was out of the question; moreover we had an autopsy and found no tumor outside the lung. However, the thyroid, a frequent source of papillary adenocarcinoma, was not examined. If the tumor was primary, it seems to be essentially a carcinoma of the alveoli with no demonstrable connection with any bronchus, and there is so little evidence that alveolar epithelium actually exists that one hesitates to make such a diagnosis. I have to leave the question open.

Dr. Sweet: From the clinical picture, I should accept the diagnosis of primary tumor of the lung much more readily than anything else. I have never seen any other case exactly like this one.

Dr. Mallory: It is very unusual for a tumor to invade an entire lobe of the lung, growing simply along the surfaces of the alveoli and producing no destruction of the lung tissue, but I have occasionally seen similar pictures before.

Dr. Holmes: What do you think of the lesions in the other lung? Were they just a red herring?

Dr. Sweet: They have not changed over a period of observation. Everyone has been looking at them and expecting them to clear up. Those who vote for tuberculosis use these lesions as evidence for tuberculosis. My opinion was purely clinical and was not based on the x-ray findings.

ADDENDUM

Between presentation of this case at conference and publication it was discovered that a papillary pseudomucinous cyst of the ovary was removed at the time of the hysterectomy. Doctor Arthur T. Hertig, of the Free Hospital for Women, Brookline, kindly loaned me a microscopic section for comparison. The character of the two tumors is identical, so I believe the major pulmonary lesion was unquestionably metastatic, and my guess is that the smaller lesions in the opposite lung must be also.—Tracy B. Mallory.

THE SECRETARY'S MESSAGE

CHIROPRACTOR LITIGATION — MICHIGAN

Circuit Judge Thomas J. Landers of Gogebic County recently handed down an opinion in litigation between a chiropractor and the Trustees of Grandview Hospital, Ironwood, Michigan.

Criminal charges were pressed by the chiropractor who claimed that the Trustees discriminated against him and wilfully neglected to perform duties while holding positions of public trust when they refused him the use of Grandview Hospital for his chiropractic practice.

Here are the salient points of Judge Landers' decision:

1. . . . "a public officer cannot be subjected to criminal prosecution for failure to perform duties which require the exercise of discretion on his part, where there is no element of an evil or corrupt design in his conduct."
2. The chiropractor "claims to be a practitioner of a school of medicine, . . . but we are referred to no statute or case where the legislature or a Michigan court has ever defined the meaning of the term 'school of medicine'."
3. . . . "To uphold the informations and force the defendants to trial in these cases would be legislating that the term "school of medicine" included a school where chiropractic was taught."
4. Under the terms of Act 350, Public Acts of 1913, the Board of Trustees were given the authority to determine rules for the hospital. The rules state that no person shall practice medicine in the hospital unless he has a license from the state of Michigan to practice medicine.
5. Charges against the trustees were dismissed.

VOLUNTARY SICKNESS AND HEALTH PROTECTION

The Health Insurance Council, comprising nine trade associations in the life and casualty fields, in its 1950 report recently released, should set socialized medicine supporters back on their heels. It is indicated that at least half of the nation's population at the end of last year was covered by one type or other of voluntary protection against the economic hazards of sickness and accident. All forms of voluntary health protection scored tremendous gains in 1950 to set new records.

Hospital expense protection, which covers the largest number of people, was extended to 76,961,000 persons at the close of 1950, 17% greater than the figure of 66,044,000 just a year before. Growing public appreciation of the advantages of voluntary health protection can be seen in the fact that the number of people protected against hospital costs has more than doubled since the end of World War II.

Great strides were also made by surgical expense and medical expense coverage in 1950. Surgical expense protection was provided 54,477,000 persons at the end of last year, compared with 41,143,000 a year earlier, an increase of 32%. A year-to-year gain of 28% was recorded by medical expense protection, which covered 21,589,000 persons in 1950, and 16,862,000 in 1949. Both surgical and medical expense coverages also have shown larger postwar gains, with the 1950 number of persons in each case being more than quadruple the 1945 totals.

The AMA Council on Medical Service has a supply of the complete insurance report and will mail to any physician requesting it.

Editorial

ARIZONA MEDICINE

Journal of

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VOL. 8 OCTOBER, 1951 NO. 10

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

LOST — ONE MILLION

It is estimated that there are one million undiagnosed diabetics in the United States. This is approximately one out of every one hundred and fifty individuals. It is primarily the responsibility of the medical profession to find these persons before they are crippled and their lives destroyed by this chronic, destructive disease.

The American Diabetes Association has spon-

sored and helped organize a continuous national diabetic drive for the past three years. This organization, which is composed primarily of physicians, warrants the support of the entire medical profession in its attempt to detect the unknown diabetics. This is the only broad health education and case finding program which has been developed exclusively by the medical profession.

DIABETES WEEK—NOVEMBER 11 to 17, 1951. This week has been set aside as a time to put forth concentrated special effort to find the unknown cases of diabetes. This "drive" and the organization itself are unique in that they are not fund raising campaigns. The American Diabetes Association has not, and does not intend to, sponsor any general solicitation of funds. The materials for conducting the campaign will be furnished without cost to authorized organizations upon request. This organization will furnish printed instructions on how to Organize a Successful Diabetic Detection Drive, Posters, Radio and Newspaper script, as well as the chemicals necessary to carry out large screening programs.

The execution of this drive is vested in the State and County Medical Societies, and all those who participate will render a needed public service.

It is not necessary that one be a part of an organized group to make this detection drive a success. Each individual physician, with little effort, can on his own part carry out a detection program which in the end would be of great value. Every physician, irrespective of the type of practice in which he is engaged, should direct all his patients to have a urine test for sugar at least once a year, and he should instruct each patient to have tests made upon their immediate families, and to urge their friends to do the same.

The American Medical Association has endorsed "self-testing" sets. These self testing sets may be purchased by any individual from a druggist for only a few cents, if they do not choose to have the urine tested by their physician or a qualified laboratory. It is advised that the individual be instructed to test the urine one to

three hours (preferably ninety minutes) after a meal which was rich in carbohydrates.

All physicians should remember this Diabetic Detection Drive, and all are urged to discharge a public obligation by detecting these unknown diabetics, so that the disease may be controlled, complications prevented, and lives happily prolonged.

For those who may desire detailed information regarding this drive you are directed to John A. Read, M.D., Chairman of the Committee on Diabetes Detection; American Diabetes Association, Inc., 11 West 42nd Street, New York City, 18, N. Y.

L.B.S.

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PAMPHLETS

Pamphlets available for distribution on request to Central Office:

Your Doctor—Association publication.

Socialized Medicine Is No Bargain—by William L. Hutcheson, A. F. of L.

Government Medicine — Danger Ahead!—by Dave Beck, A. F. of L.

A Doctor For You—AMA.

What About This Doctor Shortage?—Reader's Digest.

A FREE BATH

The British government, under its health program, already supplying false teeth, eye glasses and wigs through taxation, has decided to deliver motorized baths to the front doors of residents in a southern England town as an experiment in its program of increasing the wealth of the common man. A government truck with hot water, tubing, pump and a bath tub will call and provide the facilities.

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AMA DIRECTORY

Frank V. Cargill, Editor, reports 13,000 new names, 70,000 changes of address, and 6,000 deletions because of death, since publication of the last edition of the AMA Directory.

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GOVERNOR'S CONFERENCE

November 9 and 10—1951 Governor's Conference on Children and Youth, Phoenix College, Phoenix, Arizona. Representative delegates from religious, educational, professional, lay and youth groups, in a workshop-panel-plenary session type of conference, will meet in a state-level effort to "follow through" on the recent National Midcentury White House Conference for Children and Youth.

TOPICS OF CURRENT MEDICAL INTEREST

RX, DX, AND DRS.

By GUILLERMO OSLER

We are proud to have received a contribution from far off New York. An alert public relations firm (Noyes and Sproul, Inc.) sent some reprints which comment on the composition of FROZEN CONCENTRATED ORANGE JUICE. . . . The stuff is nearly as valuable as fresh O. J., they say, and it loses almost none of its ascorbic acid content. It also contains considerable inositol, tho no great amount of any other vitamin. . . . Thus, the New Yorkers have made a paragraph for us, acceptable to all readers EXCEPT those from Arizona and California (the juice came from Florida), and Harvard men (the chemistry was determined at Yale).

Twenty cases with scrotal or rectal PELLAGRA FROM PENICILLIN therapy were all cleared dramatically by 100 mgm. of nicotine acid, T.I.D., orally.

A NON-SPECIFIC VITAMIN THERAPY effect has been described in the American Journal of

Clinical Endocrinology. . . . Premenstrual tension has been markedly relieved by 100,000 units of Vitamin A twice a day during the two weeks before menses. The nervous symptoms, abdominal pain, and edema were variably relieved, but a high per-cent of those with mastopathies (adenosis, cysts, etc.) obtained relief.

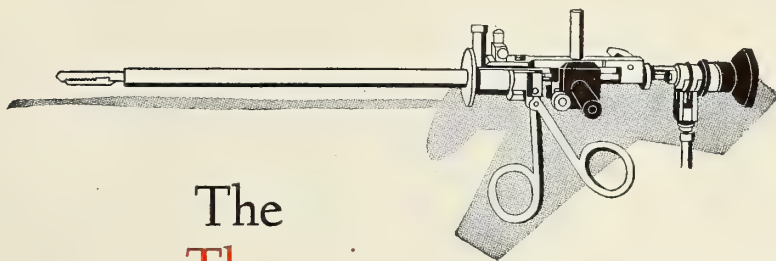
The addition of a 10-bed TUBERCULOSIS UNIT to the Pinal General Hospital is a step in the right direction. It calls attention to the relatively small number of beds for the disease in Arizona. . . . The recent public health sentiment for isolation of the tuberculous fits in which the practice elsewhere; quarantine or compulsory hospitalization has long been quietly accepted in California, Wisconsin, etc. . . . The fallacy of hoping to hospitalize Arizona's tuberculous lies in the lack of places to put them. Which 5 or 10 per cent would you hospitalize?

ACTH seems to work well in BRONCHIAL

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The Thoracic Surgeon . . .

will find aureomycin of benefit in the complications of pneumonias refractory to other forms of therapy, particularly in those very serious forms caused by the staphylococcus or by *Klebsiella pneumoniae*. In the pneumonic involvements of psittacosis, tularemia, rickettsial disease or mucoviscidosis, aureomycin is highly effective. It is also very useful in the ambulatory or surgical management of bronchiectasis. Multiple lung abscesses have been known to heal with aureomycin treatment alone. In operative thoracic procedures, aureomycin is invaluable.

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Capsules: Bottles of 25 and 100, 50 mg. each capsule. Bottles of 16 and 100, 250 mg. each capsule.

Ophthalmic: Vials of 25 mg. with dropper; solution prepared by adding 5 cc. of distilled water.

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ASTHMA. The numbers of patients in the series reported so far are not large, but one or more courses of treatment will give partial to complete relief in almost all bona fide cases. . . . The effect occurs in 2 to 20 days, using 250 to 1,000 mg. per course. Success may be estimated by the suppression of eosinophilia. The usual methods of therapy can usually be discontinued in 1 or 2 days. . . . The mechanism of ACTH effect is speculative, but asthma may be due to poor adaptation to stress, with a resultant failure of the pituitary to stimulate the adrenal cortex, and a replacement of the deficiency by the ACTH.

Dr. Edith Lord of Phoenix recently gave a paper on a topic which included the word 'Rorschach'. The announcement in a bulletin made it read 'Ronschaeh'. . . . It is probable that the printer knows the same amount about ink-blots as most doctors, or even most editors.

The new and fashionable disease this summer is 'CAT-SCRATCH FEVER'. Several reports have appeared from such separate areas as Paris, France, and Boston, Mass. . . . Greer and Keefer describe it as a lymphadenitis, accompanied by malaise and fever, following a cat-scratch. . . . The organism is obscure, but probably a virus. . . . The disease is self-limited. No specific therapy is known, tho aureomycin shortens the illness. . . . Anti-cat people might say that we could dispense with cats as a preventive measure.

The most widely and recently quoted COMMENT BY A PHYSICIAN is that of Dr. Richard Kern of Temple Medical School. He spoke on geriatrics at the San Francisco session of the A.A. of G.P. . . . "No one will admit that he is old until the fact is perfectly obvious to everyone else. Therefore, the doctor who limits his practice to geriatrics would probably starve to death". . . . Graduates of Pennsylvania, circa 1930, need not worry yet about their age, but they may remember Dr. Kern as an instructor who always gestured with his long middle-fingers.

Parsons and Wellman of Mayo's report that GASTRO-INTESTINAL IRRITATION from aureomycin or terramycin may be eliminated by,—1. Aluminum hydroxide gels (except that they decrease absorption of the antibiotics); 2. Milk (unless it is not allowed in the diet, or not tolerated); 3. Sodium bicarbonate (or certain other antacids).

While most of the CANCER RESEARCH people plug along on their various leads, one group is full cry on the True Trail. They are sure that virus-like organisms are to be found in cancer cells, the blood of cancer patients, etc. . . . One of the most certain of these is Dr. John Gregory of Pasadena. He builds his castle of theory on a

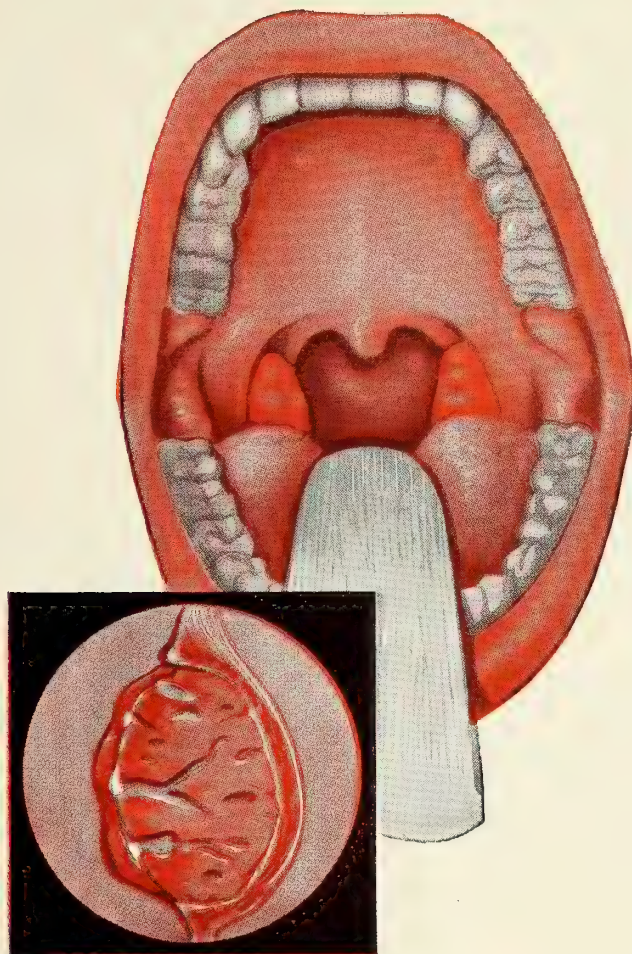
foundation of animal evidence. There is no question to him that cancer is an infectious disease caused by a virus. . . . It makes one feel stodgy and reluctant to wait for further data, but why don't the rest of the experts get in line?

German experience has shown that children with military (hematogenous) tuberculosis must be treated by STREPTOMYCIN INTRASPINAL-
LY to PREVENT meningitis. The drug passes the barrier from blood to spinal fluid poorly, even when the meninges are inflamed, and intramuscular administration is not a sufficient prophylactic.

Collier's Magazine splashes the story of Adenosine-5-Tri Phosphate all over its issue of September 1, 1951. The lead-article is called "HAS SCIENCE FOUND THE SPARK OF LIFE?". . . . ATP is not well understood; it has only been used in a number of small series; and the material is costly. The early results are favorable in such a wide variety of cases that SOMETHING might come of it. . . . It is supposed to be necessary for growth of seeds, absorption of nutrition by plants, and conversion of meat into amino acids. It is responsible for muscular contraction, for transmission of intelligence, and for such odd things as the light of fireflies and the current of electric eels. . . . The Collier's description includes a heavy charge of physiology for the general public. It describes the work being done on the substance, the symposia being held on its composition and effects—including the attention of three former Nobel Prize winners. . . . While looking for its best usage, several groups have reported it to be of value in pruritis of Hodgkin's, varicose veins, and diabetes; in bursitis; in multiple sclerosis; in senile loss of memory; and possibly in certain heart diseases. . . . Awfully early, but Collier's is there first—and can't be expelled from a medical society if it doesn't work.

Many physicians are becoming more and more cautious in their use of PENICILLIN. The hazards are definite, and Gilman believes that they are increasing. . . . The simple urticaria of year is now being replaced by a serious serum sickness, suggesting that the allergic response may now be ANAPHYLACTOID in character.

The seroflocculation TEST FOR MALIGNANT DISEASE of the chest, reported by F. X. Byron of LOS ANGELES, should be observed for a number of reasons. First, it had a fair incidence of specificity. Second, a test as this is needed. Third, Dr. Byron came to Tucson in 1946, considered the possibility of remaining there in the practice of chest surgery, but returned to Ann Arbor where he continued to run the department while Drs. John Alexander and Cameron Haight were unwell.



in acute tonsillitis:

"Excellent" responses, typical of the results obtained in a wide range of respiratory infections, Terramycin-treated, were noted in acute tonsillitis cases "within 48 to 72 hours, with rapid subsidence of temperature and physical findings."

Sayer, R. J.; Michel, J.; Moll, F. C., and Kirby, W. M. M.: Am. J. M. Sc. 221:256 (March) 1951

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ANTIBIOTIC DIVISION



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BACITRACIN has been given parenterally with success at Louisiana State. It is combined with 2 per cent novocaine. About two-thirds of the cases did very well. Some of the cases had pain at the hypo site, and some had transient albuminuria. Fifteen to 20 per cent more of the bacterial strains were sensitive to bacitracin than to penicillin.

TIME Magazine (It's a good medical journal too.) reports that a Navy doctor has a neat rule of thumb for judging the **PROGNOSIS OF ATOMIC-RADIATION VICTIMS**.—all who do not vomit should live; half of those who stop vomiting within a few hours will live; and all of those who continue to vomit will die. . . . **TIME** also mentions that three Cleveland Clinic workers have found that brain and nerve tissue can produce a hormone-like substance which enters the blood and **RAISES THE BLOOD PRESSURE**. They have an antidote called hydrazino-phthalazine. . . . A similar discovery a dozen years ago by Dr. Page of Cleveland excited the medical profession; the led-down occurred when the anti-vasotonic substance could not be produced.

GIANTS GONE.—Every now and then the mortality rate of great men seems to rise. We have lost two justly famous ones this spring. . . . Dr. George Dock faded away in Pasadena after more than ninety interesting years. A colleague of the original Osler, he was a full professor in four of the greatest American medical schools. . . . Dr. Ludwig Hektoen was a great Chicago teacher, pathologist, and editor—best known for 'The Journal of Infectious Diseases'.

CHANGING FACES AND PLACES.—We usually accept changes in teaching positions, especially if they are promotions. Dr. Gordon Meiklejohn was elevated from an assistant professor at California to the top job at Colorado; he deserved it. Dr. Nathan Womack has changed from head of surgery at Iowa to the same job at North Carolina (He was once a prof. at Washington in St. Louis). Dr. Carroll Birch shifts from Illinois to New Delhi, India, where she will be dean and trainer of deans. . . . In the surprise class is the move of Dr. Perrin Long of Johns Hopkins to the new College of Medicine at the State University of New York, and the move of Dr. Burgess Gordon from clinical professor of medicine at Jefferson to the presidency of the Women's Medical College of Pennsylvania. . . . An equally surprising move, and of special interest to Arizonans (since he came from Tucson), is the change which Dr. John R. Mote made from Armour Laboratories, where he was medical director and assistant general manager, to the medical directorship of Smith, Kline and French Laboratories in Philadelphia. Armour, ACTH, and Mote had seemed to be inseparable.

The author of this column listed some of the reportorial aims when the column first appeared. One or two of them have been mentioned since then. . . . At the risk of boring the readers, we say that accuracy as well as speed is desirable—but no person can be omniscient in this age of prolific publication. . . . Therefore, A COLUMN MUST BE A FORUM, WITH READERS ADDING OR CORRECTING IF THEIR SPECIAL KNOWLEDGE MAKES IT POSSIBLE. Please do.

• DOCTOR •

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PLAN NATIONAL MEDICAL CIVIL DEFENSE CONFERENCE

CHICAGO—The three most important persons in medical civil defense planning from each state will be brought together here November 9 and 10 in a national medical civil defense conference, the first of its kind.

The conference in the Palmer House will be held under the joint sponsorship of the American Medical Association, the American Hospital Association and the Association of State and Territorial Health Officers. State public health officers, chief hospital administrators and representatives of the state medical societies will meet with government civil defense authorities.

Among the topics to be discussed will be biological warfare, national blood program, survival during and after atomic attack, casualty medical records and community organization of life-saving teams of doctors, nurses, hospitals and others to meet disaster.

The speakers will include Millard F. Caldwell Jr., federal civil defense administrator and former governor of Florida; Col. William L. Wilson, assistant civil defense administrator in charge of health and welfare; Dr. Norvin C. Kiefer, director of special weapons defense for the Federal Civil Defense Administration, and Dr. Herman Hilleboe of Albany, New York state health officer who planned and set up New York's medical civil defense program.

Dr. James C. Sargent of Milwaukee, chairman of the A.M.A. Council on National Emergency Medical Service, will preside.

Note: Dr. Joseph M. Greer of Phoenix will represent the Association at this meeting.

THE ANATOMY BOARD

On Wednesday, October 10, 1951, Governor Howard Pyle appointed the following members to serve as a State Board of Anatomy, in accordance with Chapter 144 of the laws of Arizona, all members of which shall be appointed by and serve at the pleasure of the Governor without compensation, except the Chairman.

James P. Ward, M.D., Phoenix, Chairman (Director of the State Department of Public Health)

William N. Henry, M.D., Wickenburg

William J. Johnson, D.D.S., Phoenix

Leroy Picard, Professor of Health and Physical Education, University of Arizona, Tucson
Dr George H. Maughan, Associate Professor of Zoology, Arizona State College, Tempe

—o—

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Dr. Roy Hewitt, prominent Tucson physician, gave a paper on the application of Intermittent Positive Pressure to respiratory cripples. According to Dr. Hewitt the administration of Oxygen is given patients without regard for the expulsion of Carbon Dioxide resulting in failure of the Therapy.

He recommended Intermittent Positive Pressure breathing in cases of Bronchial Asthma, Pulmonary Edema, and Intermittent Positive Pressure with aerosol for chronic bronchitis, pneumonitis, bronchiectasis, lung abscesses and silicosis.

Mr. Lauck of the Dye Medical & Oxygen Supply Co. was on hand to explain the technical phases of the MSA Pneophore mentioned as very effective and economical for this treatment in Dr. Hewitt's talk.

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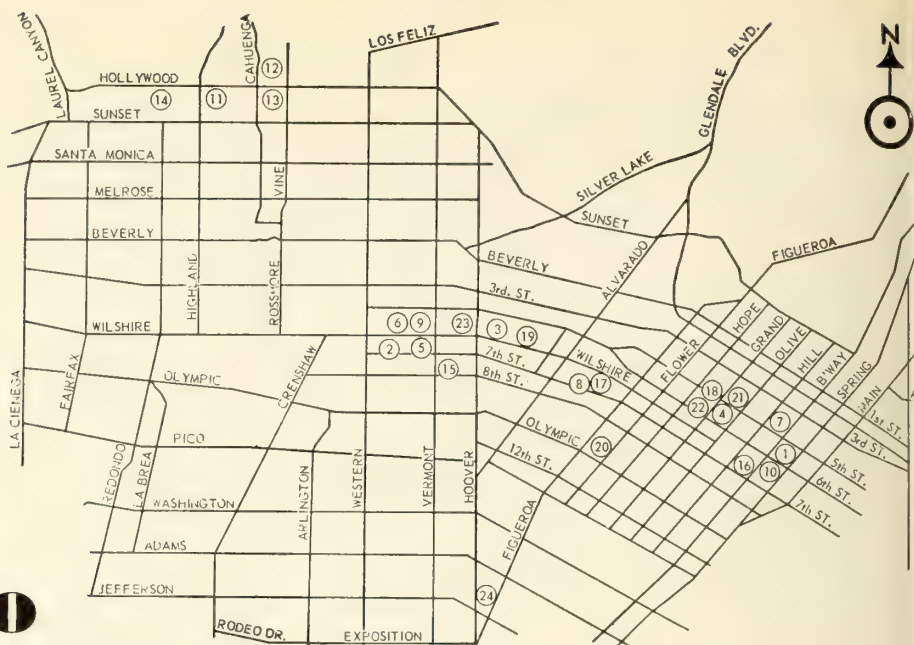
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Remember, there is no registration fee. All members of the A.M.A. are admitted free of charge. Use the hotel reservation and advance registration forms on these pages. Do it now and mark your calendar for Los Angeles, December 4 to 7, 1951.

NOTE: All reservations are to be cleared through the Local Subcommittee on Hotels. Contacting individual hotels will be useless as your application will in any case be referred to the Subcommittee. Use the form at the bottom of the opposite page, addressing the Chairman, American Medical Association Subcommittee on Hotels, 1151 South Broadway, Los Angeles 15, California.

Register in Advance Using This Application

Please fill out this coupon in full and return it at once to the American Medical Association, 535 North Dearborn Street, Chicago 10, Illinois, and receive your registration identification card for the Los Angeles Session.

I, ...
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Full name of each guest. Please do not include a physician as a guest. Every doctor must register in his own name.

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December 4 to 7, 1951

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7.	Clark.....	4.00- 5.00	5.00- 6.00	6.00- 7.00	7.50- 9.00
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9.	Gaylord.....	6.00 up	8.00 up	8.00 up	10.00 up
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17.	Mayfair.....	4.50 up	6.50 up	7.50 up	9.00
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VETERANS' LEGISLATION

In view of the staggering volume of veterans' legislation enacted since 1914 it might be of interest to review the history of this legislation because the laws then enacted have set public policy. The present Veterans' Administration stems from the old Bureau of War Risk Insurance established by Congress in 1914. The purpose of this law was to provide temporary insurance for the export shipping trade of the U. S. The insurance covered vessels, their cargoes and their passage money. In 1917 this law was amended to provide insurance for members of the military or naval forces, provide allotments and family allowances, and compensate for death or disability resulting from personal injury suffered or disease contracted in the line of duty. In addition the compensation for disability was augmented by medical care and hospitalization. The appropriation in 1917 was less than \$200 million—contrast this with the 1951 when the appropriation was nearly \$6 billion!¹ From these small beginnings the Veterans' Administration has emerged. Seven years after the Bureau of War Risk Insurance had been established, it was abolished by Congress and the Veterans' Bureau was established as an independent bureau reporting directly to the President. In 1924 the World War Veterans Act opened all hospital facilities under the control and jurisdiction of the Veterans' Bureau to honorably discharge veterans of the Spanish American War, the Phillipine Insurrection, the Boxer Rebellion, and World War 1 provided such veterans would sign a pauper's oath. Such a statement, under oath, must be accepted by the Veterans' Administration "as sufficient evidence of inability to pay." Shortly thereafter the caseload showed 80 per cent of cases to be nonservice-connected. For several years after the enactment of the 1924 law Congress showed its generosity by granting more and larger pensions. They even went back into the Indian Wars (1817). Each year Congress also authorized appropriations for construction of more hospitals and other facilities for veterans.

In 1933, in the Roosevelt Economy Act, we find a rider creating a joint congressional committee to investigate the operation of the laws

and regulations relating to the relief of veterans of all wars. The President was authorized to issue regulations regarding the amount of pensions to be paid to veterans, fix the rates of payment for disabilities and death, and to knock out all nonservice connected medical care. However, Congress did not stick by its economy. One year later the status of veterans was restored to what it had been. World War II saw a tremendous expansion of veterans' benefits. The GI law undertook a vast program of readjustment for all GIs, whether disabled or not. Job training, unemployment benefits, and a wide range of loans were made available. A great hospital construction program was instituted. At present H. R. 313 calling for the construction of 16,000 additional beds has passed the House and is before the Senate. This number of beds are not needed for service-connected cases as 88 per cent² of general medical and surgical cases are nonservice connected. H.R. 3193 provides increased pensions for disabled veterans requiring attendance of other persons including nurses. The bill applies to disabled veterans whose disability is not service-connected. This bill passed Congress but President Truman vetoed the measure and stated his opposition to any new legislation giving assistance for nonservice disabilities. The house overrode his veto by a 318 to 45 vote!

There are nearly 19 million veterans—approximately one-eighth of the population. We are likely to be kept in a state of war or near war for a long time and before long most of the youth of the country will have veteran status. Are the tax payers willing to pay this bill?

1. The Budget of the United States Government—V. A. 1951 appropriation \$5,816,674,800.

2. Administrator of Veterans' Affairs, Annual report, 1950.

Sarah S. Hirsch

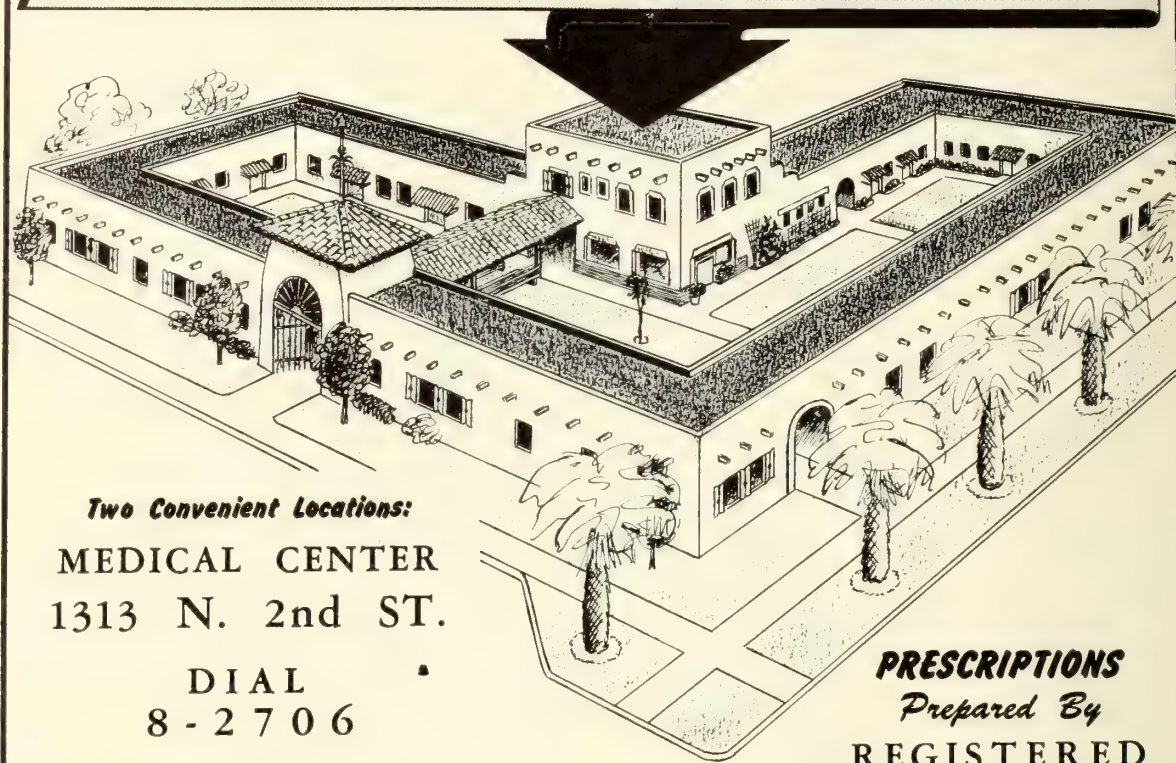
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WHAT "TODAY'S HEALTH" MEANS TO YOU!

Many of you have noticed and read the rash of popular medical articles that have been appearing in current women's magazines. According to some of our husbands there is a wealth of misinformation in these articles half-truths wild claims and historical inaccuracies. In order to increase circulation and appeal to the lay reader, these pseudo-scientific medical writers must necessarily dramatize their subject and appeal to the sensational and the gullible. Considerable mischief is created and much time spent in explaining the half-truths and misconceptions gleaned from these popularized articles. Most doctors have had the experience of having a patient bring in a clipping or an excerpt from one of these articles and demand that this new treatment, or whatever has been advocated, be instituted on him or some member of his family.

Many articles on the welfare side of socialized medicine have been published recently. These have reported the American public to be medical indigents, except for the very wealthy and the very poor. They have presented only the side of the welfare state planners and have, in general, put the medical profession in a bad light.

One of the publications of the American Medical Association, that the Woman's Auxiliary is very much interested in, is "*Today's Health*," successor to "*Hygeia*." This magazine has articles of general interest about maintaining health, various diseases, child care, surgical operations, etc., that are written or are edited by doctors of medicine. They are factually correct, unglamorized and present information in an interesting manner that doctors would like to have their patients obtain. In addition, many articles stating the profession's side of socialized medicine and giving the lie to the false claims of the social planners appear regularly.

It is in the interest of the medical profession to have this type of publication circulated among their patients as widely as possible. It is the Auxiliary's desire to bring this about and indeed is, and has been, one of our projects for many years. Considerable energy is expended in selling subscriptions to "*Today's Health*" with the principle idea of helping our doctors in mind. However, the County Society Auxiliaries compete for a cash prize in obtaining the most

subscriptions.

This year we have adopted a plan giving a subscription to "*Today's Health*" as a Christmas gift and suitable gift cards will be available. When a member of the Auxiliary contacts you for a subscription or renewal for your office waiting room, she is trying to bring about a better understanding through this publication between you and your patients; to present the true picture of the various diseases that all patients are interested in and like to read about and to help the Auxiliary in the subscription competition. It is hoped that all of you doctors will have one or more copies available in your reception room and are taking a personal subscription to peruse in your home to see what good this magazine can do for your patients. Christmas gift subscriptions are an easy and worthwhile way of remembering your select patients and it is our hope that you will keep us busy writing these orders this Christmastime.

For the benefit of the doctors and doctor's wives in communities where there is no County Society or Auxiliary, a letter or a postal card to me will insure your subscription or gift subscription promptly. The subscription price is nominal being \$1.50 for one-year, \$2.50 for two-years, and \$3.25 for three-years to physicians, dentists and Auxiliary members. The Auxiliary has made many gift subscriptions available to schools and other institutions and plans to continue these donations through the coming year.

Mrs. Paul B. Jarrett, Chairman
Today's Health

501 E. Pasadena, Phoenix, Ariz.

S.1328, SURVEY OF SICKNESS

The American Medical Association opposes S.1328, 82nd Congress, a bill to provide for a survey of sickness in the United States, on the basis that several similar studies are now proceeding under the auspices of responsible groups. The Commission on Chronic Illness was established in the spring of 1949 for the purpose of studying the entire subject of chronic diseases, including a comprehensive survey of the extent of such diseases and the programs, federal, state and local, being conducted to meet their needs. This study is now in the process of being extended for a period of three to five years and is being supported financially by a large number of voluntary health organizations

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and by the Public Health Service of the Federal Security Agency.

The Brookings Institution is also in the process of making a study of the health resources of the United States and its report should be ready for publication soon. There is little doubt that most of the information that would be developed through the operation of S.1328 has already been gathered by the Brookings Institute for its study.

A new commission for the study of hospital financing has been established this year, with financial support from several philanthropic foundations, which will conduct a three year survey in this important field. Included in its study will be the problem of chronic illness with special reference to the cost of hospitalization.

The American Medical Association does not presume to question the right of the Congress of the United States to make a study of any problem in order to provide information, on the basis of which suitable legislation can be drafted. It objects to this survey however since it is apparent that the problem is being carefully studied by several reliable commissions or agencies which will be happy to make their findings available to the members of the Congress. This new proposed survey would overlap existing studies and constitute an additional federal expense that is not now necessary.

BOOK REVIEWS

"Spatial Vector Electrocardiography, Clinical Electrocardiographic Interpretation." By Robert P. Grant, M.D., National Heart Institute, Bethesda, Md.; and E. Harvey Estes, Jr., M.D., U. S. Naval Hospital, Bethesda, Md. 41 Figures; 149 pages; June 1, 1951. \$4.50. The Blakiston Company, Philadelphia 5, New York 22, Toronto 2.

The problem of reading and interpreting electrocardiographs is simplified for practitioners and students in this text by the use of vector methods. It is written in simple and non-technical terms for daily use by those who have had no special training in physics or mathematics.

It contains only those theoretical aspects absolutely indispensable for a clear understanding of the clinical application of ECG.

The use of vector methods gives simple, accurate and objective interpretations of normalities and abnormalities. When combined with the "pattern" and empirical methods, it makes the interpretation objective rather than intuitive.

The material included covers the ventricular ECG— a discussion of the QRS and T abnormalities.

CONTENTS

Preface.

Part I, The Spatial Vector Method of Interpretation. The Vectors of the Heart; The Limb Leads as Vector Measurements; The Precordial Leads as Vector Measurements; The Method of Calculating the Spatial Vectors from Conventional Leads.

Part II, The Clinical Application of the Spatial Vector Method—The Characteristics of the Spatial Vectors in the Normal Subject; The Abnormal ECG; Abnormalities of the QRS Vectors; Abnormalities of the T Vector; The Vectors in Myocardial Infarction; The Ventricular Gradient; Broader Implications of the Spatial Vector Method. Bibliography. Index.

"Practical Clinical Psychiatry"—7th Edition. By Edward A. Streckler, Litt.D., L.L.D., M.D., Professor of Psychiatry, School of Medicine, University of Pennsylvania; Franklin G. Ebaugh, M.D., Professor of Psychiatry, University of Colorado, School of Medicine and Director, Colorado Psychopathic Hospital; and Jack R. Ewalt, M.D., Professor of Neuro-Psychiatry and Administrator of Hospitals, University of Texas Medical Branch, Galveston. Section on "Psychopathologic Problems of Childhood" by Leo Kanner, M.D., Associate Professor of Psychiatry, Johns Hopkins University School of Medicine. 35 Figures; 14 Tables; 506 Pages; June 13, 1951. \$7.00. The Blakiston Company, Philadelphia 5, New York 22, Toronto 2.

This seventh edition of a standard text for psychiatrists has been brought completely up-to-date with modern psychiatric teaching and thought.

Written by recognized leaders in the field, it is also designed for medical students and general practitioners who, because they treat the vast majority of psychiatric patients, need to keep abreast of modern developments.

The Armed Forces Classification of Mental Disorders as well as the American Psychiatric Association Classification of Mental Disorders is included. There is a new section on Support Therapy which outlines effective methods of treating patients requiring treatment less extensive than orthodox analytic procedures.

New case histories are included throughout to illustrate the basic principles.

CONTENTS

Preface to Seventh Edition; Personality Development and Function; Methods of Psychiatric Examination; The Organic Reaction Type; Toxic Psychosis; The Affective Reaction Types; The Schizophrenic Reaction Types; The Constitutional Psychopathic Inferior; Reactions of Developmental and Constitutional Defects; Paranoid Reaction Types and Paranoia; Traumatic Reactions; Psychoneuroses; Psychosomatic Medicine; "Support" Psychotherapy; Pathologic Drinking; Psychopathologic Problems of Childhood; Index.

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Among the problems of convalescence and of preoperative and postoperative care, adequate protein nutrition assumes vital importance. Such is indicated by the observation that a deficiency of but one essential amino acid in the diet of the normal individual quickly leads to an acute amino acid deficiency syndrome characterized by appetite failure, weight loss, and malaise.

Animal studies have forcefully demonstrated the adverse effect of inadequate protein nutrition on recovery processes.¹ Protein-depleted rats fed an adequate repletion ration manifest a rapid recovery of lost weight, of normal plasma protein and hemoglobin levels, of certain enzyme systems, and of normal capacity to synthesize antibody protein and to resist infection. On the other hand, reduction in the amount of but one essential amino acid in the repletion ration quickly causes loss of appetite, diminished food consumption, and inadequate weight recovery. This quick appearance of overt symptoms due to a shortage of an essential amino acid contrasts sharply with the delayed appearance of symptoms induced by deficient intake of any other essential nutrient.

These manifestations of acute amino acid deficiency noted in the rat can occur as readily in the normal human subject consuming a diet lacking in any one of the eight essential amino acids.² Loss of appetite and of body nitrogen accompanied by malaise quickly results. Furthermore, addition of the missing amino acid to the diet quickly restores the appetite, nitrogen equilibrium, and the previous state of health. Apparently, even in normal persons, lack of an amino acid in the diet partially or completely interrupts protein synthesis as well as increases tissue protein catabolism.¹ The conclusion is incontestable, therefore, that adequate protein nutrition is vital for speeding the processes of recovery from massive disease or major surgery.

Meat—all varieties and cuts—richly provides protein containing all the essential amino acids which are needed for the repair of traumatized tissue, the upkeep of normal tissue, and for other vital uses. Furthermore, meat is a dependable dietary source of iron and the vitamin B complex—riboflavin, niacin, thiamine, pyridoxine, and the newly discovered B₁₂. In health and in illness, meat ranks high as an important factor of the well-balanced diet.

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The Seal of Acceptance denotes that the nutritional statements made in this advertisement are acceptable to the Council on Foods and Nutrition of the American Medical Association.



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ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 11



NOVEMBER, 1951

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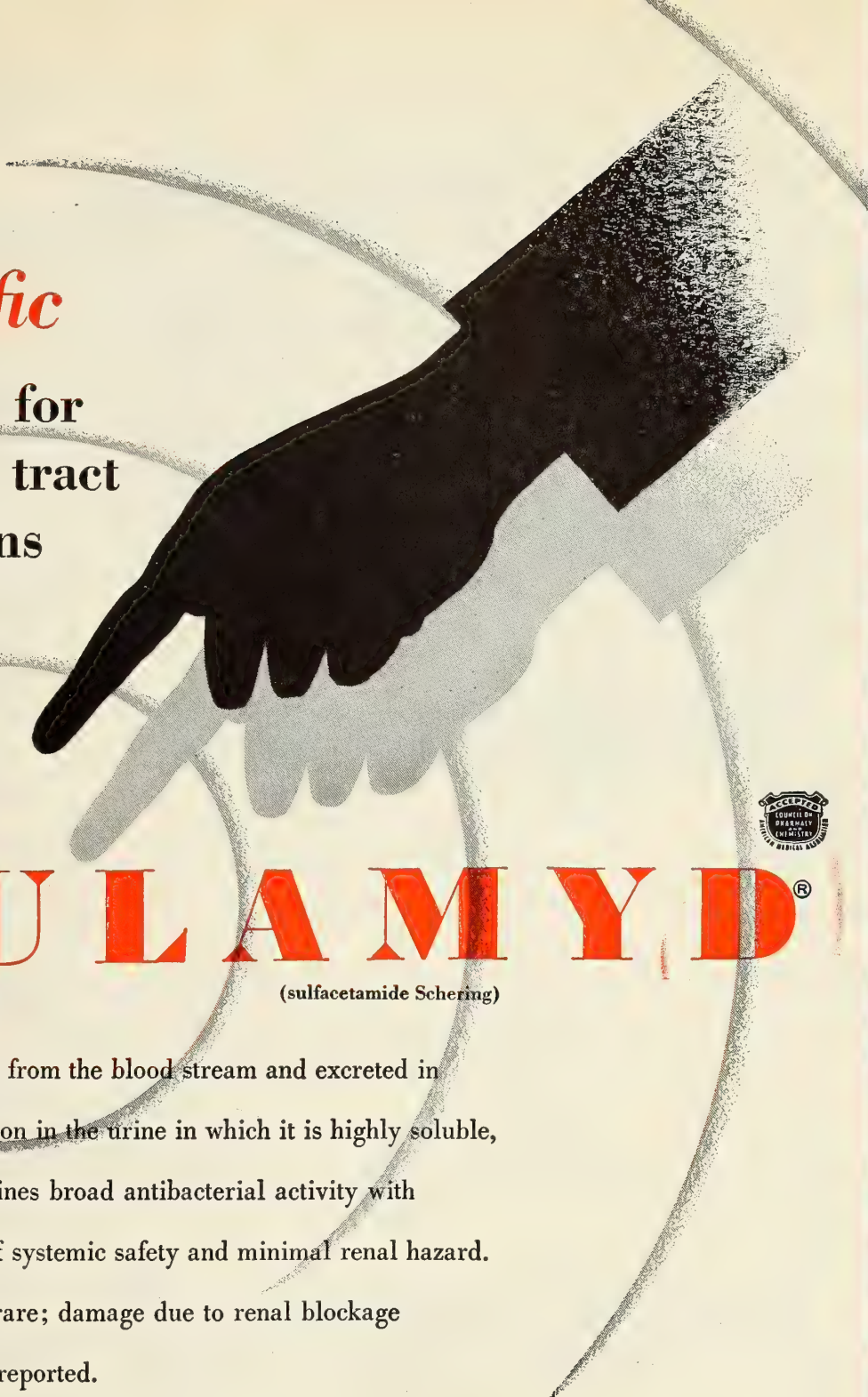
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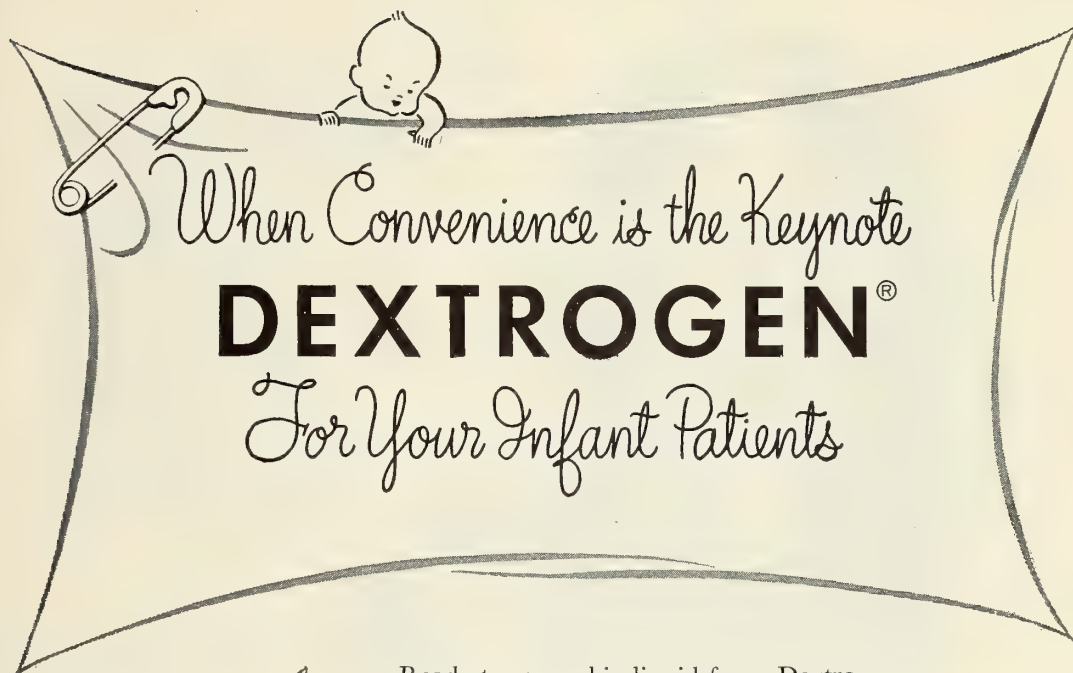
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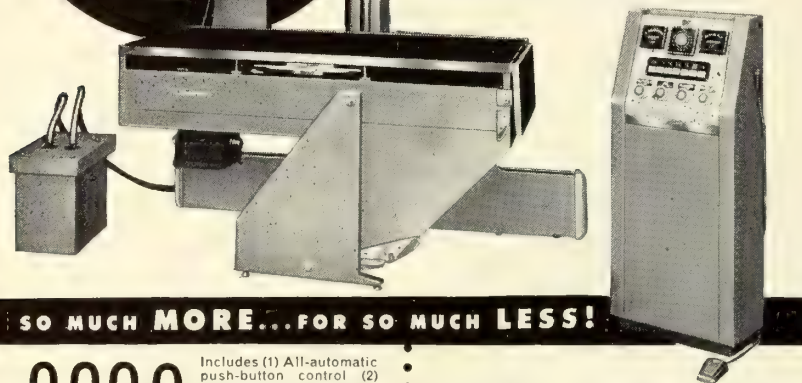


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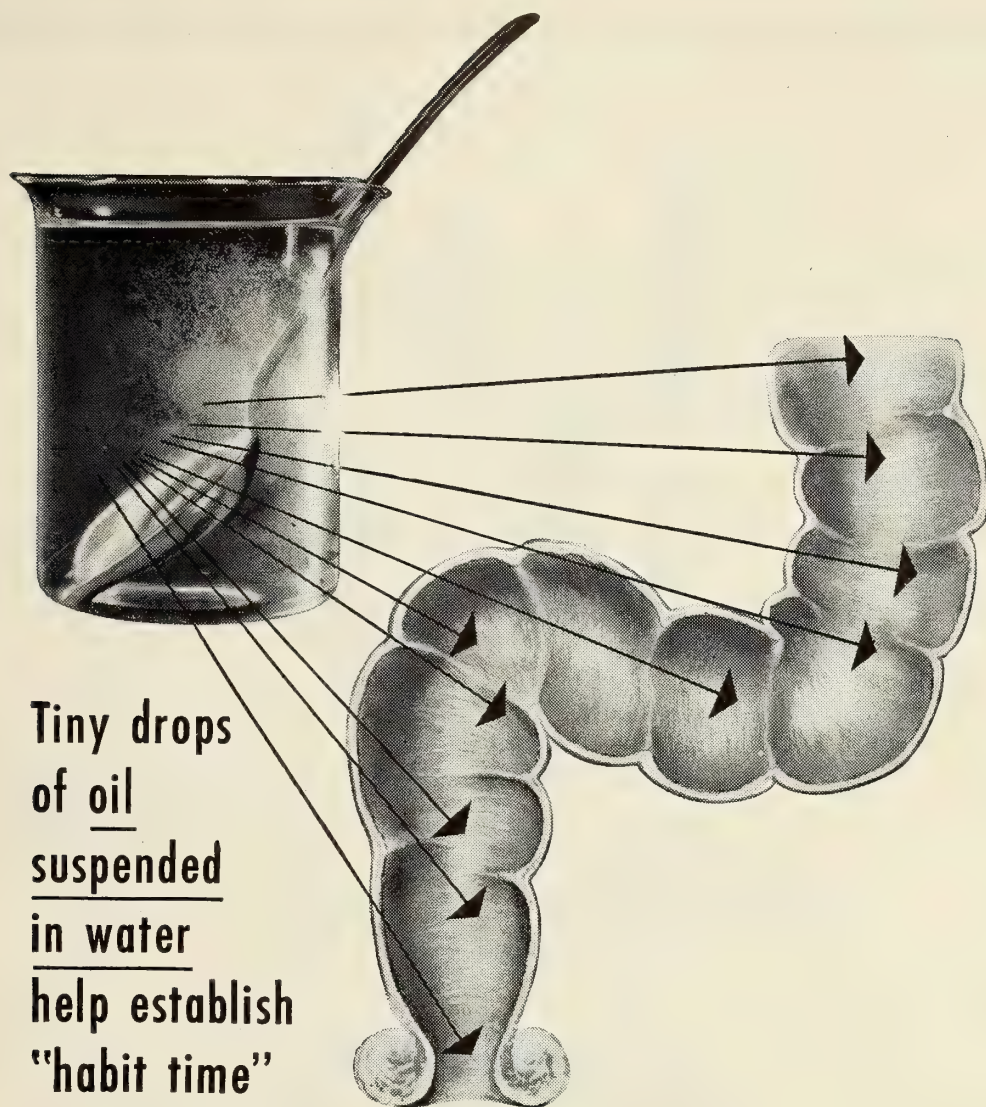
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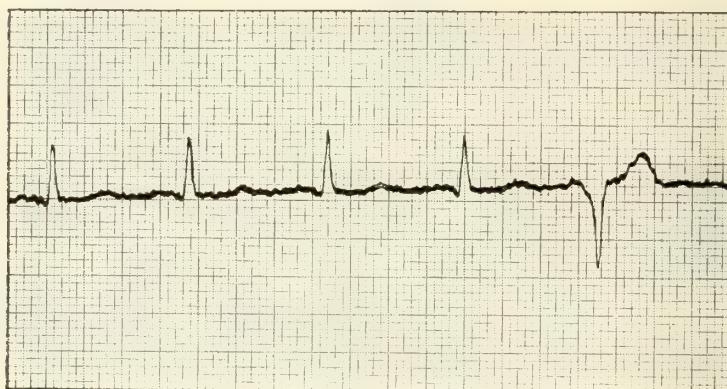


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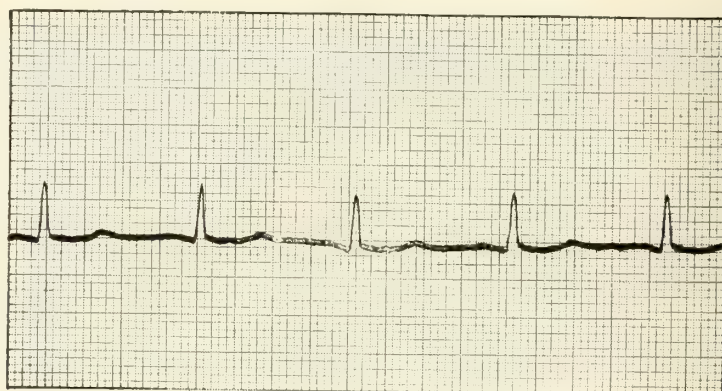
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References

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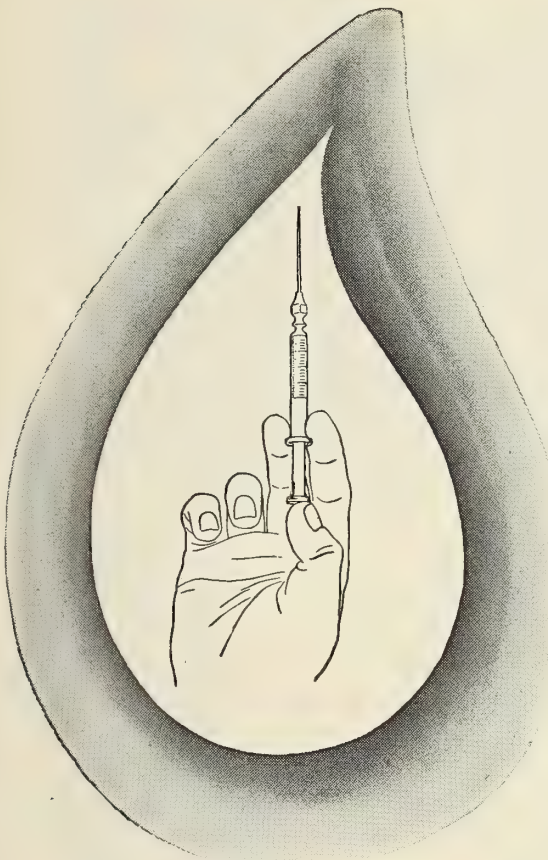
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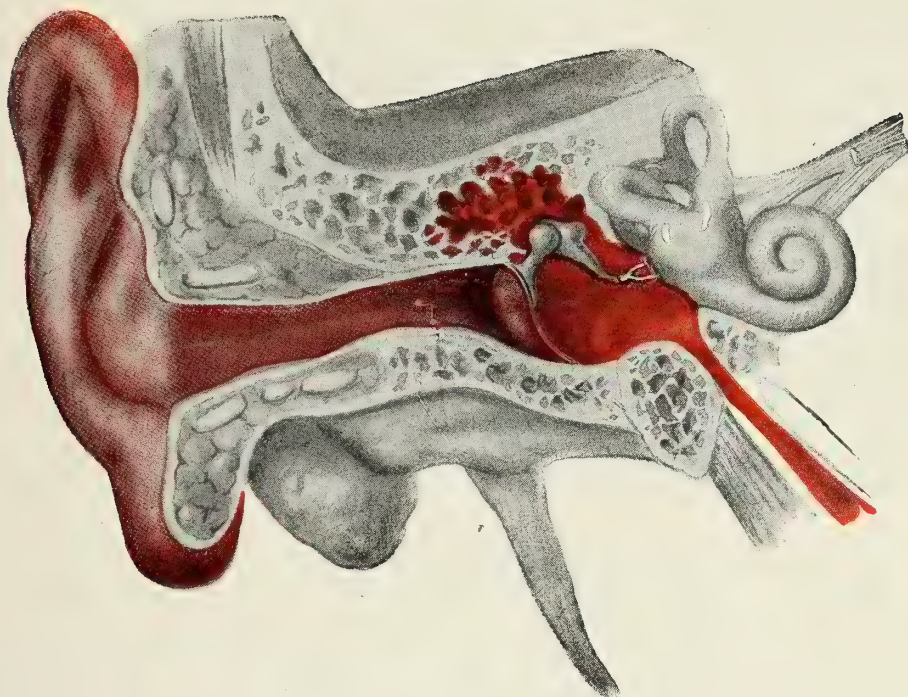


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Relationship of Stress to Autonomic Lability

Studies in psychosomatics have shown that functional disorders often are a result of the patient's inability to adjust to emotionally stressful situations (stressor factors).

Nervous tension and chronic anxiety, discharged through a labile Autonomic Nervous System, can cause somatic disturbance.^{1,2} Such states may involve any one of the organ systems or several at one time.^{1,3} The outline below is designed to relate gastrointestinal and cardiovascular symptomatology to the exaggerated response of the autonomic nervous system.

	Physiologic Effects of Autonomic Discharge	
	Sympathetic	Parasympathetic
Gastro- intestinal System	Hypomotility Intestinal Atony Hyposecretion Reduced salivation	Hypermotility Gastrointestinal spasm Hypersecretion
Cardio- vascular System	Rapid heart rate Peripheral vaso- constriction	Slow heart rate Vasodilatation
Functional Manifesta- tions	Palpitation Tachycardia Elevated blood pressure Dry mouth and throat	Heartburn Nausea-vomiting Low blood pressure Colonic spasm

The data here tabulated is from references 3,4,5,6,7, given below.

When the clinical picture is suggestive of functional disorder, the diagnosis is supported by the presence of the following indications of autonomic lability:

Variable Blood Pressure
Body Temperature Variations
Changing pulse rate
Deviations in B. M. R.
Exaggerated Cold Pressure Reflex
Oculo-Cardiac Reflex Abnormalities
Glucose Tolerance Alterations

Therapy in these cases is directed toward: 1) relieving the somatic disturbance to prepare the patient for psychotherapy*; 2) guidance in making adjustment to stressful situations and correction of unhealthy attitudes.

*Drug treatment using adrenergic and cholinergic blocking agents in conjunction with sedatives.^{8,9,10.}

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NOVEMBER, 1951

Original ARTICLES

SURGICAL TREATMENT OF ESOPHAGEAL LESIONS

DONALD L. PAULSON, M.D.

Dallas, Texas

Rapid advances have been made in the field of esophageal surgery during the last decade. It is now possible to perform satisfactory one stage procedures for a variety of esophageal lesions including congenital atresia with tracheoesophageal fistula, acquired tracheobronchoesophageal fistulae, acquired perforation or rupture of the esophagus, stricture, diverticula, cardiospasm, benign tumors and carcinoma. The aim of the surgical procedure utilized for any of these lesions is to establish esophagogastric continuity so that the patient can swallow his food in as normal a manner as possible. Ten years ago radical surgical procedures on the esophagus were either unheard of or looked upon with fear and discouragement because of the attendant high mortality and morbidity. Today it is possible to resect short segments of the esophagus and perform an end-to-end anastomosis, to resect any length of the esophagus including almost the entire esophagus and to perform a high intrathoracic or cervical esophagostomy, to perform an end-to-end anastomosis for a congenital esophageal atresia, to remove diverticula in a one stage operation and to perform various plastic procedures for stricture.

Congenital Anomalies of the Esophagus

The most common congenital anomaly consists of an atresia of the esophagus associated with a tracheoesophageal fistula. Either the atresia or tracheoesophageal fistula may be present alone in the absence of the other. Rarely, an esopha-

geal web may be present occluding the lumen. There may be an agenesis of the distal esophagus.

The diagnosis of congenital esophageal atresia associated with a tracheoesophageal fistula is easily made. The usual story is that of a newborn infant who breathes poorly and coughs and chokes on its own saliva or on attempts at feeding. In such an infant the passage of a small catheter into the upper esophagus will prove an obstruction. This may be visualized under the fluoroscope. One may readily introduce lipiodol into the proximal esophageal segment by means of a catheter (Fig. 1 A). Barium should never be used. The presence of air in the stomach and intestines when a blind upper segment is present proves a tracheoesophageal fistula. If air is not present in the stomach and intestines, but a blind upper esophageal segment has been demonstrated, one is dealing with either an atresia without the tracheoesophageal fistula or the distal segment of the esophagus is represented only by a cord. A tracheoesophageal fistula may be present in the absence of an atresia. In such an infant the catheter will pass normally into the stomach. However, instillation of lipiodol into the esophagus with the infant in the prone position will demonstrate a tracheoesophageal fistula.

Inasmuch as a congenital atresia with a tracheoesophageal fistula is incompatible with life, immediate surgery is indicated. The surgical treatment consists of first, division of the tracheoesophageal fistula and secondly, the establishment of normal continuity of the esophagus. This can usually be done in a one stage opera-

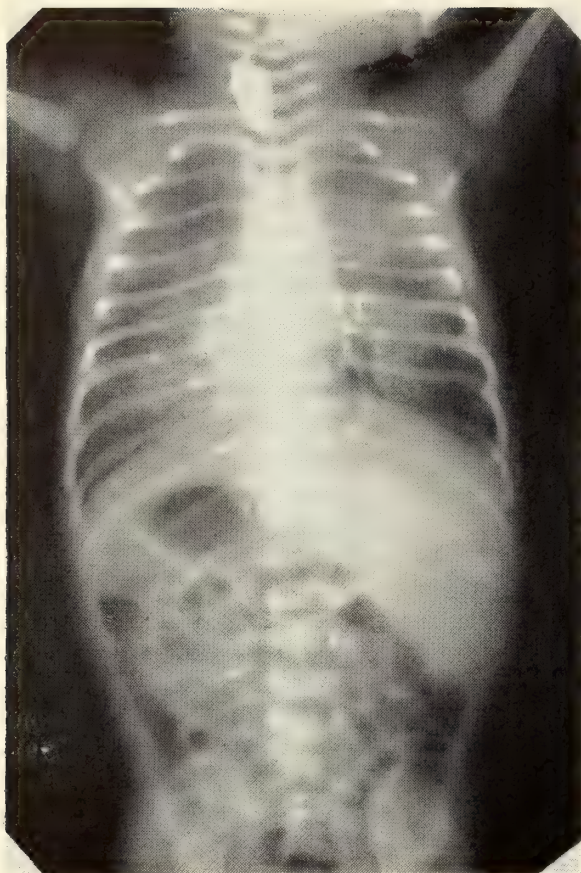


Figure 1A

tion in which an end to end anastomosis is performed between the esophageal segments after division of the tracheoesophageal fistula (Fig. 1 B). In those instances in which either the atresia or the tracheoesophageal fistula is present alone the problem is easily handled surgically. In a few instances the gap between the esophageal segments is so long as to preclude an end to end anastomosis or the distal segment may be represented only by a cord. In such instances, the tracheoesophageal fistula should be divided and the proximal esophagus brought out above the clavicle anteriorly as an esophagostomy. At a later date esophagogastric continuity can be re-established by using a jejunal transplant or performing a high intrathoracic or cervical esophagogastronomy.

Gastrostomy for feeding purposes should not be done until the tracheoesophageal fistula has been divided due to the danger or regurgitation of gastric contents into the tracheobronchial tree.

Acquired Tracheoesophageal or Bronchoesophageal Fistulae

Acquired tracheoesophageal or bronchoe-



Figure 1B

sophageal fistulae may be secondary to trauma such as caustic burns of the esophagus, the erosion of tuberculous glands into these structures, or carcinoma. Those fistulae secondary to caustic burns or the erosion of tuberculous glands may be corrected surgically (Fig. 2B). If the fistula has not been present long enough to produce pulmonary suppuration, simple division of the fistula is usually sufficient to effect a cure. If a stricture of the esophagus is present a plastic procedure or resection of a portion of the esophagus may be necessary to establish normal esophagogastric continuity. If pulmonary suppuration has occurred due to a fistula of long standing, pulmonary resection may also be indicated. In those cases in which the fistula is secondary to the erosion of a tuberculous gland the patient usually gives a history of the expectoration of small hard particles which consist of pieces of a calcified lymph node. A simple division and repair of the fistula usually is sufficient in these cases.

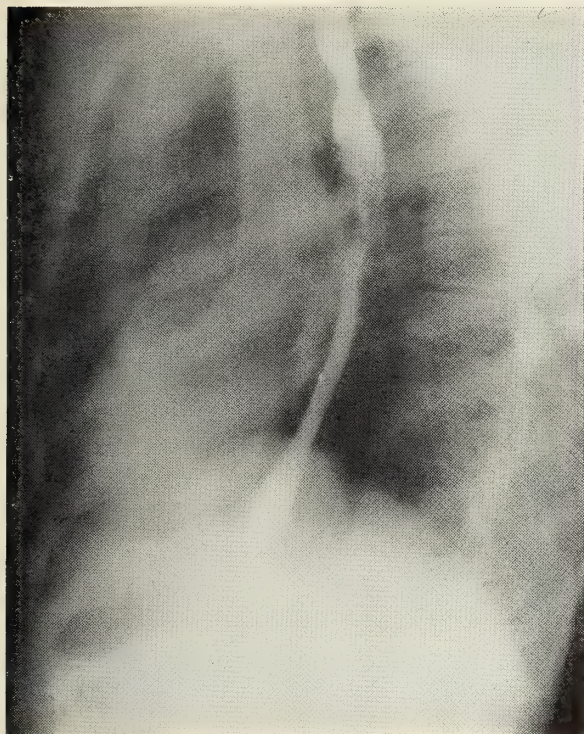


Figure 2B

Benign Acquired Stricture

Acquired strictures of the esophagus are usually secondary to caustic burns, peptic ulceration, trauma, surgical procedures and tuberculous glands. The stricture may be partial or complete (Fig. 2C & 4A). Surgical treatment is indicated in those cases which do not respond well to the more conservative measures such as dilatation. Various plastic procedures, local excision with either end-to-end anastomosis or esophagogastrostomy, or esophagogastrostomy without excision may be carried out. In certain instances resection of the esophagus and the substitution of a piece of jejunum for it may be done.⁽¹⁾

Perforation or Rupture of the Esophagus

Spontaneous perforation of the esophagus is not a rare condition judging by the frequency of reports recently made in the literature. Perforation of the esophagus may be spontaneous in a presumably normal esophagus, it may be secondary to trauma following the ingestion of a foreign body or a surgical procedure such as dilatation, or it may be due to perforation of a peptic ulcer. The esophagitis associated with a diaphragmatic hernia may antedate the perforation. The patient's history is very important in determining the cause of the perforation. The history of ingestion of a foreign body

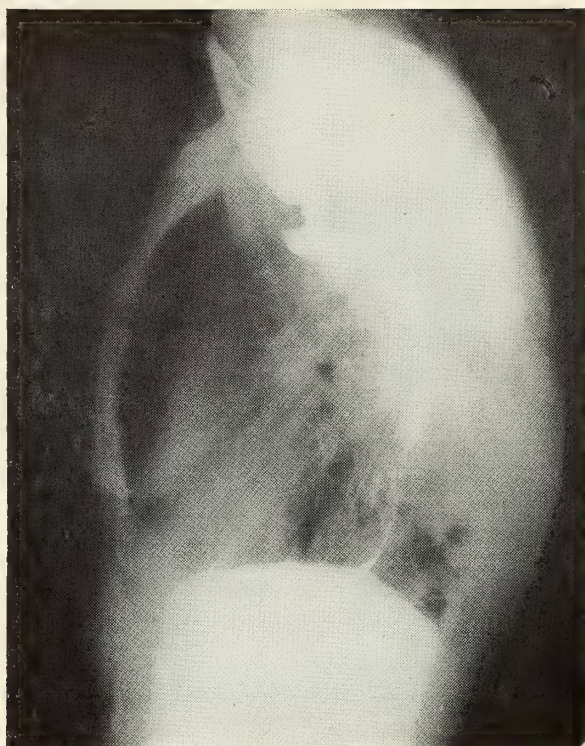


Figure 2C

or operative manipulation will establish trauma as the cause. The previous history of symptoms of ulcer of the esophagus or of an esophagitis associated with an esophageal hiatal diaphragmatic hernia should make one suspicious of the underlying cause. In most of the cases of spontaneous perforation of the esophagus reported in the literature there has been no background in the history that would suggest disease of the esophagus.

Although the symptoms and findings differ according to the cause any esophageal perforation produces mediastinitis and not infrequently an empyema also. Prompt surgical attention is necessary in addition to the liberal use of various antibiotics. The diagnosis can readily be made on the basis of the history and the roentgen findings. These latter will reveal air or fluid within the mediastinum behind the heart or in the neck. A swallow of radiopaque oil with fluoroscopic observation may be demonstrate the esophageal perforation (Fig. 4B).

The treatment of esophageal perforation varies with the cause, the size of the perforation, and the duration. In any case the mediastinitis or empyema must be treated by drainage. If the perforation is seen early, whatever its cause may be, operative closure of the opening in the esophagus may save the patient a long and

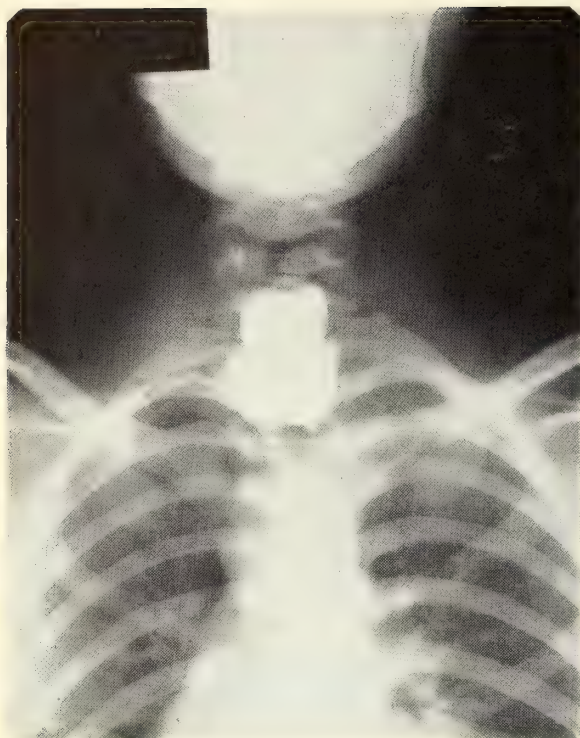


Figure 4A

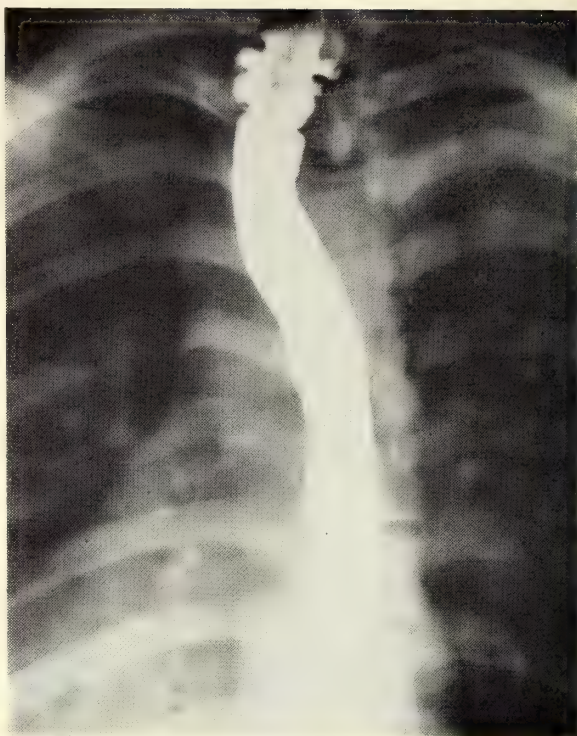


Figure 4B

severe illness.

Spontaneous perforation or rupture, presumably in a normal esophagus, usually occurs during vomiting, most frequently after a bout of alcohol ingestion. These perforations are usually very large and the mortality almost 100 per cent if treated conservatively. The treatment of choice consists of prompt thoracotomy, wide opening of the mediastinal pleura, closure of the esophageal defect, adequate drainage of the mediastinum and closure of the chest with intercostal tube drainage.⁽²⁾ This procedure must be carried out in spite of the patient's poor condition. The large opening in the esophagus leads to a rapidly extending mediastinal infection which can only end fatally in a short period of time. Attempts to drain the local infection by mediastinotomy or pleural drainage during the acute stage have generally been unsuccessful in the case of spontaneous perforation in a presumably normal esophagus.

Diverticula

A diverticulum of the esophagus may be pharyngoesophageal or epiphrenic in location. The traction diverticula due to a tuberculous gland or trauma may be located anywhere along the extent of the esophagus. Diverticula vary as to size and extent but as time goes on they usually progressively enlarge.

The weight of the diverticulum and its contents pull it in a downward direction so that it narrows or compromises the normal esophageal passage. Its own opening progressively enlarges. A varying amount of inflammation occurs in the wall of the diverticulum and ulceration and perforation may occur as complications. One stage surgical removal can now be done with a high degree of success without fear of mediastinitis. (3)

Cardiospasm

In those cases of severe cardiospasm or achalasia of the esophagus in which repeated dilatation of the esophagus does not produce the desired results or in those cases in which pulmonary complications or severe anemia are complications, a plastic procedure at the esophago-gastric junction to enlarge the opening may be indicated and can be done transthoracically at a low risk.

Benign Tumors

Benign tumors of the esophagus are relatively uncommon. They may be divided into two main groups—the mucosal and the extramucosal tumors. The mucosal tumors are pedunculated and arise from the submucosa. Usually they are fibrolipomas or fibromyxomas covered by normal epithelium. The extramucosal tumors arise from the muscle of the wall of the esophagus.

gus and usually do not involve the mucosa. These are commonly leiomyomas.

Growth of these tumors is usually slow and therefore they may attain considerable size before giving rise to serious symptoms. Symptoms produced by these tumors are dysphagia, pain, regurgitation of food, cough and dyspnea. A pedunculated tumor may be regurgitated itself into the mouth. The diagnosis is readily made by the roentgenographic and esophagoscopic examination of the esophagus.

Although the indications for surgical treatment of benign tumors are not as urgent as for malignant lesions of the esophagus, surgical removal is indicated. These tumors are usually large when first seen, and therefore act as a mediastinal tumor by compressing the esophagus and the adjacent mediastinal organs. It is considered possible that these tumors may undergo malignant change. The pedunculated tumors may be readily removed through a cervical or transthoracic esophagotomy. The intramural tumors may be shelled out from the wall of the esophagus preserving the intact mucosa, the wall being reconstructed after removal of the tumor. In a few instances the mucosa will be damaged in the removal of the leiomyoma which may necessitate a resection and an anastomosis.

Small pedunculated tumors may be removed through the esophagoscope by means of a snare and cautery.

Esophageal cysts do occur and may be readily removed. They produce symptoms by pressure on the esophagus and adjacent mediastinal organs such as various parts of the tracheobronchial tree.

Carcinoma of the Esophagus

Cancer of the esophagus is of more frequent occurrence than are all malignant tumors of bone and is even more common than cancers of the lip, tongue, larynx or kidney. It constitutes about 4 per cent of the deaths in cancer of the esophagogastrintestinal tract in the United States (Gastric cancers 56%)(4) and 5 to 10 per cent of all carcinomas in males, being surpassed in frequency only by carcinoma of the stomach, lung and rectum. Until ten years ago, there was justifiable pessimism concerning esophageal cancer. Surgical procedures available were mutilating and were staged procedures. Very often the patient died from his cancer before the surgical plan of attack could be completed. The first successful resection and esophago-

gastric anastomosis for esophageal cancer was reported by Adams and Plemister in 1938.(5) During the ensuing ten years, this operation has been extended and modified so that now it can be applied in the treatment of carcinoma of the esophagus at all levels with the exception of the cervical segment. The morbidity and mortality of this surgical procedure have reached acceptable low levels. Although sufficient time has not elapsed for a statistical study of end results, reports which are available (6) suggest that carcinoma of the esophagus treated by radical resection will behave like carcinoma elsewhere in the body (lung and stomach) and that there will be enough cases of three to five year survival to justify the use of the operation in the hope of effecting a cure. Because of the pitiable plight of the patients who are unable to swallow because of complete esophageal obstruction, it is justifiable to make an effort to remove the cancer in every case, however hopeless the prognosis may seem. One of the major benefits of the operation is the restoration of esophagogastric continuity and the ability of the patient to swallow food. Many such patients may live in relative comfort without any recurrence of dysphagia for as long as two or more years after resection and an esophagogastronomy.

The obscurity of symptoms all too frequently results in a late diagnosis. Most patients coming to surgical treatment have had dysphagia for a period of six months or more. The medical profession as a whole must be alert to the possibility of esophageal cancer in order to make the diagnosis early. Any patient with dysphagia deserves careful roentgenographic and esophagoscopic investigation before any treatment is instituted. These two diagnostic procedures will readily reveal the presence of an esophageal carcinoma.

The surgical procedure utilized for a carcinoma of the esophagus varies according to the region where the tumor lies. The restoration of continuity after resection of a carcinoma in the cervical segment of the esophagus requires the substitution of a turned in portion of skin for the excised portion of esophagus. This may be accomplished by the method described by Wookey.(7) If the carcinoma is located in the upper fourth of the thoracic segment (in the superior mediastinum) a one stage esophageal resection with a cervical esophago-

gastrostomy is performed by means of two incisions. Through a left thoracotomy incision the entire esophagus from the base of the neck to the cardia is dissected free and resected. The thoracic incision is closed and a second incision is made over the lower cervical region anteriorly. The esophagus is dissected out through the incision, the fundus of the stomach being brought up into the cervical region from the chest, and the esophagogastric anastomosis is done within the neck above the level of the clavicle actually in the subpharyngeal region.

A carcinoma in the middle half of the esophagus (extending from the superior border of the aortic arch to the inferior pulmonary vein) is treated by esophageal resection and a high intrathoracic esophagogastronomy. Whether the anastomosis is done superior or inferior to the aortic arch, depends on the location of the tumor. Any cancer which lies at least in part behind the aortic arch requires a high level of resection in order to remove the cancer adequately. Esophageal carcinoma characteristically extends submucosally so that wide resection is advisable in an effort to extirpate the disease.

A carcinoma in the lower fourth of the thoracic segment—that is that portion lying between the inferior pulmonary vein and the stomach—

is treated by resection of the esophagus and a portion of the stomach lying along the lesser curvature and a low intrathoracic esophagogastronomy. Without pathological examination it may be difficult to determine the exact origin of the tumor whether it be esophagus or stomach. From a practical standpoint, however, the operative technique is the same in either case.

Summary

As a result of rapid advances in the field of esophageal surgery in the last decade, it is now possible to perform satisfactory one stage procedures for a variety of esophageal lesions including congenital atresia with tracheoesophageal fistula, acquired tracheoesophageal fistula, acquired stricture, perforation or rupture of the esophagus, diverticula, cardiospasm, benign tumors and carcinoma.

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CHOLECYSTECTOMY WITHOUT DRAINAGE

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This is not a new subject. In 1906, Witzel(16) of the Berlin Clinic reported 500 cases of cholecystectomy without drainage and yet today, 40 odd years later, cholecystectomies are routinely drained in many hospitals. One looks back not so many years to the day when appendectomies, cesarean sections, gastric and intestinal operations were likewise routinely drained; whereas now, with a sense of progress, one notes that as a rule the abdomen is tightly closed in these cases. Gallbladder surgery does not enjoy this same progress, yet the proponents of non-drainage cite the following advantages of cholecystectomy without drainage, namely:

1. A cleaner wound with less chance of infection.

2. Less opportunity of inducing infection into the peritoneal cavity from the outside.
3. Fewer eviscerations.
4. Fewer herniae.
5. Avoidance of persistent sinus formation.
6. Less danger of bile leakage from the stump because of the tendency toward leakage is increased by pressure of the drain on the cystic stump preventing peritoneal agglutinins from covering and scaling off the stump.

The literature contains numerous reports of cholecystectomy without drainage; however, only those series in which mortality rates are given appear here:

Note the favorable mortality in the non-drained cases in this series.

In reviewing these cases, particular attention was paid to the incidence of bile peritonitis.

"Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statement and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration."

Name	Year	Without		%	Cases With		%
		Drainage	Mortality		Drainage	Mortality	
Abell	1927	391	8	2.04%	109	2	2.00%
Bailey	1939	129	0	0.00%			
Bettman	1942	306	5	1.63%	67	0	0.00%
Bottomley	1920	19	0	0.00%			
Coventry	1923	50	0	0.00%	30	4	13.33%
DeCoursey	1933	36	1	2.77%	300	20	6.66%
Fowler	1928	240	8	3.33%	543	15	2.76%
Mallet-Guy	1947	116	1	0.89%			
Verbrycke	1927	86	0	0.00%			
Willis	1917	35	1	2.86%	69	0	
Willis	1921	41	1	2.44%			
Witzel	1906	500	1	0.02% (Bile peritonitis)			
Total		1,949	26	1.34%	1,118	41	3.66%

All of the authors made a statement that no bile peritonitis occurred in these series except the single case of Witzel's. One may ask what becomes of the bile that forms in the undrained abdomen and the proponents of non-drainage argue that it does not form as seen in the re-operated cases.

429 CHOLECYSTECTOMIES AT THE GENESEE HOSPITAL*

*Teaching Hospital Associated with the University of Rochester School of Medicine and Dentistry.

Four hundred twenty-nine cholecystectomies were performed at the Genesee Hospital from 1936 to 1946. Three hundred ninety eight cases were drained and 31 not drained.

Bile peritonitis developed in five cases resulting fatally in three instances, with a mortality rate of 60%. Two of these were in the 31 undrained cases and three were associated with common duct explorations in the drained cases. There were no instances of bile peritonitis in the drained cases when the common duct was not explored.

This series is striking in that non-drainage resulted in bile peritonitis in two out of 31 non-drained cases and in one it was fatal.

Because most cholecystectomies are drained in spite of theoretical advantages of non-drainage, it is felt that other surgeons in other institutions have had similar experience with bile peritonitis in undrained cases. It is probable that the ill effects of non-drainage do not regularly appear in the literature. The unexpected drainage of bile in the first few days following a simple cholecystectomy has often puzzled sur-

geons as to its cause. Unrecognized accessory bile ducts are incriminated. The proponents of drainage advise routine drainage to avoid an occasional fatality from bile peritonitis. Most of the older and more experienced surgeons will say that they did not drain until they lost such a case.

The following questionnaire was sent to a number of surgeons in scattered areas of the country:

1. Do you advise routine drainage of Morison's Pouch following cholecystectomy?
2. In your experience and the experience of your institution have you noticed an increased instance of bile peritonitis and complications in the undrained cases?
3. Would you care to further express ideas on the subject? *Replies appear below:*

Warren H. Cole: University of Illinois

1. "With few exceptions, I recommend and institute drainage following cholecystectomy.
2. "I have not had enough experience with closure without drainage to state whether or not this method would be followed occasionally by complications such as bile peritonitis. However, we have had one patient on whom a repair for a bile duct stricture was performed. Drainage was used but the wound around the drain was closed too tightly. This patient developed bile peritonitis, and we had to open the wound 24 hours after the operation; she ultimately died with numerous abscesses.
3. "Accordingly, I recommend drainage to protect the occasional patient. In perhaps

no more than one or 2%, will significant escape of bile from a cystic duct, aberrant hepatic duct, etc., take place."

George Crille, Jr.: Cleveland Clinic

1. Do you advise the routine drainage of Morison's Pouch following cholecystectomies? "Yes."
2. In your experience and the experience of your institution, have you noticed an increased instance of bile peritonitis and complications in the undrained cases? "Always drain."
3. "I have seen bile peritonitis or leakage when least expected. The appearance of bile from the drain gives warning of this. I always drain for two or three days."

Laurence S. Fallis: Henry Ford Hospital
(Referred by Roy D. McClure):

1. Do you advise the routine drainage of Morison's Pouch following cholecystectomies? "Yes, without exception."
2. "We cannot say that there have been increased instances of bile peritonitis in undrained cases because it is the practice in this hospital to drain patients. However, every year we have two or three cases of bile peritonitis that have been operated upon elsewhere and not drained."
3. "We readily admit that there are many instances, and perhaps a majority of the cases of clean dissection and removal of the gallbladder that the abdomen could be closed without drainage. However, we are unable to determine which case will give trouble, and therefore we advise drainage in all cases, since there is extreme variation in the amount of drainage in these patients. Furthermore, we have no instances on record in this hospital in which any complication could be directly attributed to the presence of the drain. We use the Penrose type of drain exclusively."

John H. Gibbon, Jr.: Jefferson Medical College

1. "I do advise routine drainage of Morison's Pouch following cholecystectomies."
2. "As we routinely drain, we have had no experience with undrained cases."
3. "I might say that we regard drainage with a soft filled cigarette drain as a simple precautionary measure which does not increase the length of convalescence and I can see no reason for abandoning this simple procedure."

Frank Glenn: The New York Hospital

1. "We routinely drain following cholecystectomy."

Henry N. Harkins: University of Washington School of Medicine

1. "I now advise routine drainage of Morison's Pouch following cholecystectomies. Several years ago, for a short time, I did not drain Morison's Pouch, but gave up this practice because I now work in so many hospitals that I cannot follow the cases as well as I could formerly. I had no disastrous results in the few cases where the pouch was not drained."
2. "In our experience, as already stated, we have seen no disastrous results, but we have only used the non-drainage method in a half a dozen or less cases."
3. "I am coming to the belief that when drainage is done, it should be done with a Chaffin tube arrangement, or by the sump drainage method of Babcock. Generally speaking, I use sump drainage, or Chaffin tube drainage in almost all cases where I am going to drain."

Emil F. Holman: Stanford University

1. Do you advise the routine drainage of Morison's Pouch following cholecystectomies? "Yes."
2. In your experience and the experience of your institution, have you noticed an increased instance of bile peritonitis and complications in the undrained cases? "Two deaths from non-drainage in 1922 perpetrated by another surgeon. This has forever prejudiced me against it!"

(Referred from Dr. Wangenstein):

Arnold J. Kremen: University of Minnesota

1. "It has been the practice in this clinic for some time to regularly drain Morison's Pouch following cholecystectomies."
2. "We have on several occasions seen collections of bile in the subhepatic space and even the development of subphrenic abscesses which I believe came about as a result of failure to drain following cholecystectomy."
3. "I have seen very few instances wherein drainage in this area providing the drain is brought out through a stab wound lateral to the incision, has ever caused any difficulty, and there are times when I think it has prevented postoperative complications."

F. H. Lahey: Lahey Clinic

1. "We drain down to the foramen of Winslow in all cases and have never closed a cholecystectomy without drainage.
2. "I think that we have had two fatalities from bile peritonitis in the patients who had been closed without drainage who came here late, with bile leakage and with their abdomens filled with bile. These patients had had their gallbladders done elsewhere."

Alton Ochsner: Ochsner Clinic

1. "We do not do routine drainage of Morison's Pouch or of the abdominal cavity following cholecystectomy. Drainage in our cases of cholecystectomy is dependent upon the ability to carefully cover the cystic duct stump with serosa and the presence or absence of exudation from the gallbladder bed. We believe that there is a likelihood of the cystic duct stump blowing off unless it can be covered with peritoneum which will permit the holding of fibrinous exudate around it which can become organized. Unless we can satisfactorily cover the cystic duct with peritoneum we always drain the peritoneal cavity and we also drain when there is a continued ooze from the gallbladder bed.
2. "We have not noticed any cases of bile peritonitis or complications in undrained cases when we adhere to this rule."

Herman E. Pearse: Strong Memorial Hospital

1. Do you advise the routine drainage of Morison's Pouch following cholecystectomies? "Yes."

Samuel J. Stobins: Genesee Hospital

"At the Genesee Hospital, Rochester, New York, it is the policy of the Surgical Service to drain Morison's Pouch following cholecystectomies on all Staff cases; drainage in private cases rests entirely with the attending surgeon."

Waltman Walters: Mayo Clinic

1. Do you advise the routine drainage of Morison's Pouch following cholecystectomies? "Yes."

DISCUSSIONS

Part of this paper was presented by one of the authors (CGF) at a staff meeting at the Genesee Hospital. Because of the two incidences of bile peritonitis in 31 undrained cases at that hospital, it was believed that this might

have been due to ill-chance rather than to the method. Many surgeons were privately questioned over a period of years and it became evident that other institutions had had similar results from non-drainage so that most surgeons had abandoned it in favor of drainage. It is felt the favorable data in the literature are due to selection, many of the ill results not being reported.

SUMMARY

1. Theoretical advantage of non-drainage following cholecystectomy are given.

2. The mortality rates in non-drainage are collected from the literature.

3. Four hundred twenty-nine cholecystectomies at the Genesee Hospital, in the ten year period between 1936 and 1946, are reviewed. In 398 cases which were drained bile peritonitis developed but three times and all these were associated with common duct exploration. Thirty-one "ideal" cases were not drained and bile peritonitis developed two times in this series; one proved fatal.

4. Reports of a questionnaire sent to a number of surgeons in various parts of the country are presented.

5. In spite of theoretical advantages and the available data in the literature, it is felt that young surgeons should omit drainage following cholecystectomy with a great deal of temerity.

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PERSONAL COMMUNICATION

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WHAT TO KNOW ABOUT CARCINOMA OF THE LUNG

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1. FREQUENCY:

Statistics regarding the frequency of cancer of the lung vary considerably between hospital and hospital depending upon whether the medical and surgical staffs are especially interested in it and through reputation attract a considerable number of patients of this type. Naturally, it is from those who have a special interest that most of the publications have come. I suspect, therefore, that they give a somewhat exaggerated picture of its frequency in relation to other forms of cancer. Certain it is, however, that it is one of the most frequent forms of malignant disease particularly in the male, occurring as it does, in a proportion of 6 or 7 males to one female, and as such, warrants the increasing attention that it is receiving. During the 10 year period ending 1946 in the Department of Pathology of the Toronto General Hospital the third most frequent site of primary cancer was the lung, being preceded in the list only by the stomach and large bowel.

2. ETIOLOGY:

Nothing definite is known regarding the cause of cancer of the lung. It has been attributed to the use of tar in road building but Boyd showed that it seemed to be more frequent in Winnipeg than Toronto. It has been blamed upon the inhalation of petrol fumes but seems to be as common in rural as well as urban communities. The belief that it is due to tobacco does not seem to have been well founded. Its supposed relation to previous inflammatory disease of the lung is probably due to inaccurate diagnoses. Until further evidence is produced we must regard the etiology as unproved.

3. PATHOLOGY:

The histopathology need not concern us. The important thing is that it arises in the bronchi and that it may appear anywhere in the bronchial tree. Seventy-five to 80% arise in the primary and secondary division of the bronchi, the remainder more peripherally. It spreads by way of the lymph vessels to the bronchial lymph nodes, mediastinal nodes and thence along the communicating nodes to the neck or abdomen. Widespread metastases through the blood

stream are unusually frequent. The cells probably gain entry to the blood stream via the thoracic duct or by direct invasion of veins. It is one of the most frequent sources of bone metastases. Spread to the brain through vertebral system of veins is common. Pleural effusion may be inflammatory in origin or due to extension of the cancer to the pleura. A blood-stained effusion is usually due to carcinoma. Like all other forms of cancer its rate of growth varies greatly. The most malignant forms kill the host in a few months; the occasional patient may survive for 4, 5, 6 or even 7 years without treatment.

4. SYMPTOMATOLOGY:

I believe that we have all laid too much stress upon the classical picture of cancer of the lung and in so doing made the diagnosis appear too easy. If the course of events proceeds according to what would be expected, the growth in a primary or secondary bronchus acts first as a foreign body and produces an irritating cough; next follows clear or whitish sputum from over secretion of bronchial glands, with ulceration, bleeding occurs and the sputum becomes streaked with bright red blood or occasionally gross hemoptysis is seen. When the lumen of the bronchus has been narrowed enough to interfere with the clearing of secretions distal to the area, infection occurs and the sputum becomes purulent. At about the same time atelectasis occurs in the segment of lung distal to the growth and bronchopneumonia develops. The patient has bouts of fever and if the parietal pleura is involved, pleural pain. There is often a deep-seated pain or discomfort in the chest quite apart from the pleural pain. Unfortunately this classical picture is no more to be depended upon than the classical picture of appendicitis. The important thing to remember are that the development of a cough, a change in the character of a cough blood in a sputum, a sense of pain or discomfort in the chest should not be disregarded. Recurrence of pneumonia in the same area of lung means bronchial obstruction and demands investigation. The appearance of a lung abscess or bronchiectasis in a patient of cancer age should be regarded as secondary to cancer of the bronchus until this has been

excluded. Growths which arise peripherally are unlikely to produce any symptoms in the early stages. There may be chest pain of varying character or, if the parietal pleura is involved, pleural pain. The patient who complains of feeling that there is something unusual in his chest should not be reassured because physical examination of the chest is negative without an x-ray being made.

5. DIAGNOSIS:

As in all other disease, the most important thing is to be aware of the possibility of cancer of the lung. "What one knows, one sees." A careful history is of first importance.

Physical examination of the chest may or may not yield information of significance. The early lesion, whether it be in the larger bronchi or toward the periphery, is unlikely to give rise to any change in physical signs. When, as a result of the blocking of a main bronchus, a considerable area of atelectasis has developed, there will be a shift of the mediastinum toward the lesion with diminished resonance and air entry over the area and harsh breathing. There may or may not be rales. Peripheral growths must, as a rule, be very large to be recognized clinically. In the presence of extensive atelectasis the decreased movement, decreased size of the chest deeper intercostal spaces and increased obliquity of the ribs on the affected side may be obvious. If pleural fluid has developed it, of course, gives the usual signs. No importance should be attached to the absence of changes in the physical signs.

The presence of a Horner's syndrome, of enlarged lymph nodes in the neck and axilla and enlargement of the liver should always be looked for. If an enlarged node is found it should be removed for diagnosis. If the patient is hoarse the vocal cords should be examined. A paralyzed cord usually means that the case is inoperable. Complete immobility of one leaf of the diaphragm suggests involvement of the phrenic nerve and usually inoperability.

X-ray films of the chest provide the most important single method of examination. If the growth is peripheral in location it is readily seen. In a central lesion the first change is always an area of atelectasis with slight shift of the mediastinum and perhaps elevation or depression of the hilum and elevation of the diaphragm. More extensive changes are, of

course, easily recognized. Unfortunately, widening of the mediastinum may be the most prominent finding due to involvement of the mediastinal lymph nodes. A perfectly normal x-ray film may be found but is extremely rare even in early cases. Laminographs should often be done. Good bronchograms may be very helpful either through demonstration of a definite block in a bronchus or a filling defect in the lung parenchyma corresponding to the area of atelectasis. Both of these changes may be found in the absence of new growth and must be interpreted, therefore, in relation to other findings.

A bronchoscopic examination should be done if the history is suggestive even though x-ray has been normal. In most clinics only about 50% of the cases are yielding positive biopsies. If more patients present themselves at an earlier stage this percentage is likely to become still lower. Examination of bronchoscopic aspirates and sputum for cancer cells has proved useful in many clinics. If the clinical history is suspicious and x-ray findings are suggestive, thoracotomy should be advised even though the bronchoscopic findings are negative and no cells have been found in the sputum or aspirates. Recently several patients have been operated on whose lesion was found on routine x-ray surveys in whom all other examinations were negative and who had no associated symptoms.

6. DIFFERENTIAL DIAGNOSIS:

Pneumonia, particularly of the atypical variety, since it is segmental in distribution and may be associated with some degree of atelectasis, may be most difficult to differentiate. Primary atypical pneumonia rarely persists longer than 6 weeks. In doubtful cases it may be necessary to "wait and see" for that length of time. The presence of a foreign body in the bronchus must be considered even in the absence of history. Lung abscess or bronchiectasis developing after middle life must be regarded as possibly secondary to carcinoma until proved otherwise. Hodgkin's Disease or Lymphosarcoma in the mediastinum may occlude the lumen of a bronchus and produce a secondary atelectasis and an x-ray picture quite indistinguishable from advanced cancer of the bronchus. When doubt arises a therapeutic trial of x-ray will usually solve the matter since the lymphomas are highly radiosensitive. Peripheral growths may be confused with any other type of primary growth as well as tuberculomas.

Occasionally the doubt may be overcome by an aspiration biopsy but thoractomy is usually necessary. Bronchial adenomas can be distinguished from carcinoma only on biopsy. An adenoma rarely produces an isolated parenchymal shadow. In the absence of positive sputum, tuberculosis may occasionally present some difficulty.

7. TREATMENT

Surgical removal offers the only hope of cure since these growths are highly resistant to radiation. Lobectomy may be justified occasionally but pneumonectomy is the procedure of choice. Sufficient evidence has now accumulated to prove that these growths can be cured by surgical removal. As in cancer elsewhere cure

depends on the type of disease and the time of diagnosis. Palliative pneumonectomy is worthwhile in some cases to free the patient to symptoms that arise from infection distal to the growth and in the hope of making his demise more comfortable. The prolongation of life that can be accomplished may be worthwhile but I do not believe that a mere extension of life for a few months is in itself to be considered of great value.

Radiotherapy may have some palliative effect. The prolongation of life claimed by radiotherapists must be assessed with great care since some patients live so long without therapy of any sort. With improvement in technique it is worth further trial in inoperable cases.

UNUSUAL VARIETIES OF PNEUMONIA AND PULMONARY ABSCESS

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It is the intention of this paper to point out how completely dangerous it may be to accept as satisfactory diagnosis such common nomenclature as abscess of the lung, atypical or viral pneumonia, and unresolved pneumonia.

Most of these terms come from the radiologists, and we are sometimes content to accept such a roentgenologic diagnosis without ado and immediately proceed to the use of the antibiotic with which we are currently infatuated. Prior to the days of roentgenography it was the custom to diagnose about everything that was associated with a high fever, pleuritic pain, cough and leucocytosis as pneumonia. If there were no satisfactory physical findings, it was influenza. The roentgenologists forced upon us a rather more accurate morphologic consideration of infection of the lung; they showed that disease was not always lobar or bronchopneumonic but might be segmental; that what we thought was pneumonia was often-times the inflammation of an abscess in which necrosis had not yet occurred.

Then came the first—perhaps the greatest—of the antibiotics, penicillin, and a new classification sprang up among clinicians. There were just two kinds of pneumonia then: those which responded to penicillin and those which didn't. In many places this simple classification seems to persist, though the multiplication of potent antimicrobial agents has tended to keep the

clinician somewhat more alert. In a sense, though, the classification is still somewhat the same, only a little broader: now there are infections that respond to penicillin; those that do not, but respond to some of the others; those that fail to respond to any antibiotic.

It is against such an ultra-empiric approach to disease that these remarks are delivered. There is and can be but one satisfactory approach to the problem of pulmonary infection and that approach is an etiologic one. The cases about to be shown are demonstrations of the necessity of pertinacious investigation. In this discussion it is fair to assume that two important differentials already have been carefully considered—as they should be in every instance in which a report of unresolved pneumonia, viral pneumonitis or abscess has been offered by the roentgenologist. Those two conditions are familiar and have been mentioned often: they are tuberculosis and carcinoma. Until those two diseases have been excluded, a beginning cannot be made on a pulmonary diagnosis.

But even after carcinoma and tuberculosis seem adequately excluded, there remain many other diseases that call for precise etiologic study. It is with these that this discussion deals. Just what percentage of pulmonary infection they represent is uncertain. These, of course, are called from many admissions. It probably is safe to estimate that such conditions

represent about 1% of all admissions for acute infections of the lung.

Several conditions are not represented since in the area from which these patients come there is a relatively low incidence of infestations, there is no mining and relatively slight industrial hazard and there is comparative freedom from the more exotic tropical diseases. In addition, but not included, are a number of pulmonary infections in which the most exhaustive efforts, including on occasion lung biopsy, have failed to produce a satisfactory answer.

In the majority of these unusual cases of pneumonia it is evident that they represent pulmonary complications or localizations of the less familiar infectious diseases. In a few cases the pneumonia is the result of some comparatively infrequent affection of the lung itself, while in others the infiltration of the lung may represent abnormal reaction or prior morphologic alteration of the tissue.

Table I presents a classification of pneumonias which has been found to be of value in approaching the problem of a baffling pulmonary infection.

Before proceeding into the presentation of individual cases, two further warnings should be added. So-called post-operative pneumonia or ether pneumonia, which characteristically is manifest about the third day is not primarily an infection, but is the result of bronchial obstruction. Although the condition responds to penicillin, the use of an antibiotic confuses the issue. The important step is the reopening of the occluded bronchus.

The other warning is to be on the alert for pulmonary infarction in the healthy, active individual. The roentgenologist in many instances will be unable to differentiate a subsegmental pneumonia from an infarct and physical examination not infrequently fails to reveal any evidence of peripheral venous disorders. Points of some aid in the differential diagnosis are the character of the sputum which will be mentioned later, the very dramatic onset, the relatively low temperature and leucocyte count and the early appearance of a sterile, hemorrhagic effusion (frequently seen only in lateral film). Jaundice seems not to develop unless preexisting hepatic disease is present and the electrocardiogram practically never affords a clue. A roentgenographic clue of great importance is the conversion, often within three or four days, of

the original consolidation into horizontal linear shadows which may persist for some days. Almost never does the postero-anterior or lateral film reveal a pyramidal or conical shadow.

The following cases of pneumonia illustrate varieties of unusual pulmonary disease. There are of course a group of notable omissions. Primary coccidioidal infiltrations are not encountered in the Dallas area; no proven case of infectious mononucleosis with pneumonic infiltration is included; strongyloides infestations of the lung, which seems to have been familiar to those in Burmese and Indian theatres, is missing.

TABLE I

Pneumonia of bacterial etiology.
Primary atypical pneumonia.
Pneumonia due to specific viruses.
Pneumonia of Rickettsial origin.
Pneumonia due to higher organisms.
Infections due to yeasts and molds.
Loeffler's syndrome.
Pneumonias resulting from systemic diseases.
Infiltrations associated with malignant diseases.
Pneumonia due to the inhalation of toxic gases and fumes.
Pneumonia due to inert foreign matter.

REPORT OF CASES

CASE 1. The patient was a while male of early middle age who entered the hospital with the complaint of fever, malaise, cough, headache and generalized aching. Laboratory studies were of note mainly for their lack of information. Bronchoscopy indicated a somewhat fixed and rigid intermediate bronchus on the left, but secretions were negative on Papanicolaou staining. Fever responded slowly and gradually over a period of time and it is impossible to state that any antibiotic produced a definite effect. Since the shadow persisted unchanged over a period of some time, it was considered safer to explore for carcinoma than to accept negative findings as being exclusive. The tissue grossly revealed a chronic organising pneumonia; histologically it was said to be compatible with the infiltrations characteristic of Q-fever. Serologic studies for that disease which had been weakly positive shortly before surgical exploration subsequently became much more strongly positive. (1, 2).

CASE 2. This patient, a young white male, entered the hospital with high fever and considerable malaise. On his skin there were a few small vesicles, which after two days became

much more numerous and took on a hemorrhagic character. Four days later the temperature began to subside and the patient was entirely well on the sixth day. His two children had recently been confined with known chickenpox. (10).

CASE 3. The patient, a farmer in late middle age, had been working in the fields during intensely hot weather. He suddenly became intensely ill with high fever, photophobia, marked muscular pain and cough. When he entered the hospital his temperature ranged around 103-104°, his entire body was quite tender to touch and his cough was productive of dark blood. Six or eight days later jaundice appeared. Chest taps resulted in bloody fluid. Dyspnea became intense in spite of repeated taps and oxygen. By the twelfth hospital day cyanosis and dyspnea were severe, there was intense jaundice, marked cylindruria and albuminuria and rapidly rising urea. All the common agglutination tests were negative and although the specific etiologic agent was never demonstrated we feel quite safe in presenting him as a case of Weil's Disease.

CASE 4. A middle-aged white female had been ill at home for about a week. There had been considerable cough, some shortness of breath and wheezing and a moderate degree of fever. In spite of aureomycin, she had become worse and her attending physician noted an increase in an area of consolidation. Chest film revealed a somewhat irregular consolidation. In the hospital her course was marked by temperature as high as 103, a moderate leucocytosis with persistent eosinophilia of varying degree and not always constant. The only organism recovered from the sputum by repeated culture was streptococcus viridans. When she was first placed on penicillin there was a short period of improvement lasting about four days, at the end of which the temperature which had nearly reached normal began to rise steadily. No combination of penicillin with any other antibiotic proved of advantage. When penicillin was increased there was always a short period of response. For six weeks the picture remained essentially unchanged, the patient at all times showing rather marked dyspnea, a slight violaceous cyanosis and experiencing some pleuritic pain from time to time. At last, for the want of any other satisfactory therapy, it was decided to place her on doses

of penicillin in the range ordinarily used for subacute bacterial endocarditis. On this regimen her temperature fell rapidly to normal and remained so thereafter. Some three weeks after her discharge and about nine weeks after the onset of her illness, resolution of the lower lobe pneumonia was essentially complete, when suddenly a new patch appeared in the left upper lobe. This migratory behavior seems to justify our diagnosis of Loeffler's syndrome, since eosinophilia was fairly clear throughout. If this is correct, it is somewhat unusual to find such a relationship with what was apparently a pneumonia due to streptococcus viridans. Since that time, for a period of nearly two years, the patient has been quite well.

Acute abscess of the lung is usually dismissed simply with that diagnosis. Most abscesses are of the usual mixed, anaerobic variety, the predominant organism probably being an anaerobic streptococcus. The mode of onset is usually sudden, often following a period of unconsciousness from whatever cause. The patient presents within a matter of hours the picture of severe pulmonary infection with hyperpyrexia, pleuritic pain, severe cough, dyspnea and cyanosis. Clubbing of the fingers may develop within as short a time as seven days in a few severe and large abscesses. Films up to the third or fourth day rarely reveal evidence of cavity formation, but are suggestive of abscess by the predilection of that disease for the dorsal segment of the lower lobe and for the axillary portion of the upper. From about the fifth day on—assuming treatment has been delayed for any reason—the cough becomes productive of foul sputum and roentgenograms of the chest reveal rapidly developing rarefaction, with or without fluid level.

Under present conditions many of these are aborted in the pneumonic, precavitary stage and undergo complete resolution. Either by reason of inadequate treatment or delayed treatment a certain number of patients proceeds to a modified variety of the once familiar picture. In many cases due to antimicrobial therapy, the sputum never becomes frankly putrid.

We are now particularly concerned with those patients who, having received adequate treatment, have persistent cough, sputum, fever and roentgen evidence of cavity. Here as in the case of the pneumonias one must always be sure

that tuberculosis and carcinoma have been well excluded. But even after these two prominent possibilities are clearly put aside, there remain certain other necrotizing diseases of the lungs which have to be considered. There are, of course, abscesses due to unusual organisms, mallei, bacteroides, klebsiella, and blastomycosis. Of these we have no examples, yet such diseases are probably not uncommon in certain areas. Other etiologic types are notable for their roentgen similarity to ordinary anaerobic abscess, for their protracted course and for their almost complete resistance to treatment with any antibiotic. Certain characteristics of their behavior, however, might have offered clues at earlier dates, while others even in retrospect cannot well be differentiated by any method from simple abscess.

CASE 1. A white male of early middle age went to a local tuberculosis control unit complaining of fever, cough, expectoration, malaise, loss of weight and weakness. A chest film revealed at that time (some four weeks prior) essentially the same situation evident in the slide. Although a sputum was negative upon a single examination, he was regarded as having tuberculosis and sent to the city sanatorium. He was moderately febrile, there was persistent leucocytosis, and continued cough with the expectoration of considerable amounts of yellow or greyish sputum which was always negative for tubercle bacilli. Carcinoma was included in the differential diagnosis, but bronchoscopy with cytologic study of secretions was negative. He was then considered to have an abscess and was placed on considerable doses of antibiotics, first one at a time and then in combination, all with little or no result. Numerous agglutination tests failed to afford any useful evidence. Finally wet mounts of the sputum revealed motile endamoeba histolytica, and following this cysts were found in the stool. He was treated with emetine, diiodoquin and chloroquin, the last of which produced dramatic results. The clue in this patient's case, so far as there was one, was the presence of a very slightly enlarged and moderately tender liver. Jaundice was absent and liver function tests were normal. The patient denied any symptoms suggestive of amebic colitis. (7, 8).

This case is of more than passing interest in that abscess of the lung, non-contiguous with the hepatic process is quite uncommon and

that the result with chloroquin treatment was so extremely successful. The outcome of such cases as given by Ochsner and DeBailey (6) has been marked by a high fatality rate (prior to availability of chloroquin).

CASE 2. A young colored man, known to be alcoholic, appeared at the admitting office with a temperature near 105. He was clouded mentally and at least a major part of the history had to be obtained from relatives, who stated that about two or three weeks earlier he had begun to have severe pain in the abdomen and flank, experience fever and chills, and to complain of headache. The patient was severely and acutely ill with moderate dyspnea and questionable cyanosis. Major guarding seemed to be present over the right upper quadrant. There was thought to be mild jaundice, which was confirmed by the icteric index. The day following pain shifted to the left flank and there was an increase of dyspnea, definite cyanosis and very considerable splinted cough. Two days later the cough became productive of dark red to brown, moderately thick blood. Mucus and pus were almost totally wanting from the sputum, which upon repeated examination for every type of pathogen, was negative. The patient remained dangerously ill for a period of some two weeks, at the end of which time his temperature began gradually to subside, his consciousness to clear and his cough and chest pain to diminish. He received in very considerable quantity every antibiotic available and the decline in temperature seemed to coincide with penicillin up to 3 million units per day. The chest film showed gradual clearing although the cavity remained, undergoing frequent changes in size. At the end of another four weeks the patient appeared clinically to be doing quite well and consideration of some method of procedure against the residual cavity was being taken when he suddenly sat up in bed one day, gasped and died. Autopsy revealed that the cause of death was a pulmonary embolus and that the abscess was in fact an acute, non-suppurative necrotic process involving what was originally an infarct. Acute and chronic cholecystitis was also discovered.

While this possibility was considered early in the differential diagnosis it never received the attention due it. That attitude resulted from the fact that while acute necrosis and cavity formation in infarcts is mentioned the condition

seemsto be an extremely unusual one. At no time was there evidence of circulatory disorder in the legs. Finally the history and the picture as presented at admission were strongly suggestive of an acute infectious disease in the background and Weil's Disease was rather strongly entertained for a time. If a clue existed in this case, aside from the negativity of all bacteriologic and serologic studies, it was in the character of the sputum. The jaundice, which otherwise might have helped, seemed to go better with acute disease involving the liver or gall-bladder for which there were good anamnestic and physical grounds.

CASE III. A white male in the fourth decade entered the hospital complaining of chest pain, shortness of breath and fever. Physical examination presented the usual signs of pneumothorax but otherwise was non-contributory. There was leucocytosis with a sharp shift to the left. X-ray revealed a hydro-pneumothorax, while within the lung itself was a rounded, very thick-walled cavity which seemed in the standard projection to lie just beneath the pleura. Since the patient had seen service during the war in the West Texas and in the Arizona area, a coccidioidin skin test was done and the reaction was positive. Culture of both sputum and plueral exudate resulted in ready growth of coccidioides. The patient prior to admission had had a chronic productive cough of some years duration, the sputum being rather consistently yellow in color, but non-foul.

CASE IV. A white male in the latter part of the sixth decade stated that for some three or four weeks previously he had noted fever, cough and sputum of unpleasant taste. On one occasion there had been hemoptysis of perhaps as much as 90 cc of fresh blood. The patient appeared acutely and chronically ill and the greenish, muco-purulent sputum was somewhat offensive in odor. Rhonchi were heard near the hilum and beyond this there were dullness, diminished breath sounds and a few rales. Bronchoscopy revealed no visible pathologic process other than a reddened mucosa. Secretions studied for cellular morphology were reported as showing a few atypical cells, but no definite psotive diagnosis was possible. The patient was subjected to exploratory thoracotomy after preparation with antibiotics. Grossly this was thought to be an abscess only, but dissection revealed a small tumor, which proved to be car-

cinoma, in one of the branch bronchi.

It is worth emphasizing that in the consideration of a patient in middle life who presents the picture of an abscess, it is of the utmost importance to secure a thorough history as to the mode of onset. In the event of a gradual onset, with a sputum which becomes foul only after some period of time, carcinoma is always a strong probability.

CASE V. The patient, a farmer from the east-ern edge of Texas, entered the hospital in a very acutely ill condition. He had been treated for a short period of time at his home by his local physician but when penicillin had failed to result in any improvement in his cough he was referred to the hospital. It was learned further that the patient had had an abrupt onset with a chill and high fever some ten days before, that there had been some chest pain although it was not of a violent character, and that cough had begun a day or two later and had been productive of mucoid or mucopurulent sputum which at times contained both bright red and dark brown blood. The leucocyte count was elevated and there was a strong left shift. Sputum studies were not immediately revelatory and the routine agglutinations at the time of admission were not altered to a significant degree. Blood cultures yielded no additional information. Since the patient apparently had received adequate doses of penicillin he was placed on a combination of one of the other antibiotics with streptomycin. On this therapy over a period of some days his temperature gradually subsided and significant clearing of the consolidation occurred. As the patient became better able to cooperate it was learned that he frequently went hunting in the woods and had killed and skinned both squirrels and rabbits. A repetition of the agglutination studies for tularemia was strongly positive. This case is of unusual interest for although pulmonary manifestations of tularemia have frequently been reported and although one report mentions the formation of an abscess this is apparently the first case of tularemic abscess whose film has been reproduced. It is noteworthy that there is no obvious feature which would differentiate it from any other abscess so far as the film is concerned.

There has been presented today a group of acute and subacute diseases of the lung which admittedly are rather rare. The purpose of this

presentation has been to emphasize the importance of suspicion of one's own diagnosis and study. There is probably not one of this entire group of patients who might not have been correctly diagnosed earlier had a level of suspicion been sufficiently great.

For those who have studied these patients during their illness—they have been demonstrations of the ultimate fallibility of all laboratory techniques. Roentgenographically, these abscesses and these pneumonias were not distinctive. From the standpoint of the clinical laboratory all usual studies were contributory only indirectly. In fact, until the suspicion of the correct diagnosis had been entertained and the laboratory was able ultimately to confirm these suspicions all valued tests merely served for exclusion.

On the other hand what has been demonstrated is the importance of searching clinical thought and study. In one instance the occupation, in another the habits, in a third the kind of sputum, in a fourth an apparently unrelated hepatic tenderness, in a fifth an evanescent rash contained the luminescent key to the problem.

What all this seems to point to is that the competent clinician must have constantly in mind the patterns of behavior of all the more common varieties of pneumonia and abscess and must cultivate an acute sensitivity to the abnormal behavior of a disease process. He must bear constantly in mind that the film of the chest may reveal only a chance localization of a generalized disease and must avoid the pitfall of mistaking a part for the whole. And above all else the clinician must remember that a careful history, a good physical examination and some close observation will lead more frequently to correct diagnosis than a tremendous multiplication of laboratory tests.

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BASIC *Science* SEMINAR

THE PHYSIOLOGY OF CELLULAR RESPIRATION, INCLUDING CARBON DIOXIDE AND OXYGEN EXCHANGE

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INTRODUCTION

Cellular respiration is defined by Reid (1) as those biological processes and cellular mechanisms by which the cell converts the bound radiant energy of the sun, stored in foodstuffs, to free utilizable biotic energy, thereby making possible cellular activity and even cellular existence. At once this definition limits the present discussion to those metabolic processes taking place within the cell, and excludes the more familiar phase of oxygen and carbon dioxide exchange in the lungs and extra-cellular fluids. A discussion of the specialized oxygen and carbon dioxide carrying cells of the blood, the erythrocytes, is also eliminated because these cells serve primarily in gaseous transport. Instead, it is the plan of this paper to take up those metabolic processes that are intimately

concerned with the metabolism of cellular contents, and to show some of the fascinating and complex mechanisms by which intracellular respiration takes place.

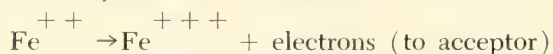
In order to discuss this topic, it is necessary for one to visualize the individual cell, surrounded by its cell membrane, and containing perhaps hundreds of complex interacting enzymes, catalyzing chemical reactions of foodstuffs or metabolites. This cell in turn must be thought of as part of a coordinated group of cells that takes part in the formation of a tissue and an organ. The problem of supplying these groups of cells with foodstuffs, oxygen, water, and of disposing of carbon dioxide and waste products is complex almost beyond comprehension. The physiology of cellular respiration concerns itself with the sum total of those chem-

ical reactions that have to do with the breakdown of cell metabolites for the release of energy required for cell work. Fundamentally these reactions are oxidations.

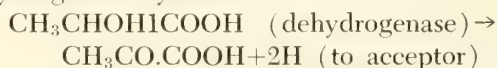
GENERAL PRINCIPLES OF BIOLOGICAL OXIDATION

In any chemical reaction, oxidation can be carried out by the addition of oxygen to a substance, by the removal of hydrogen, or by the withdrawal of electrons. In all three it is the loss of one or more electrons from the substance being oxidized that characterizes the oxidation reaction. In cellular or biological systems, four general types of chemical reactions may be recognized as oxidation reactions (2):

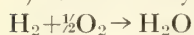
1) Loss of electrons, e.g. as found in the iron atom of cytochrome molecules.



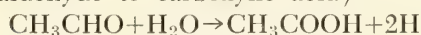
2) Loss of hydrogen, e. g. as in certain dehydrogenase systems.



3) Gain of oxygen



4) Addition of water with loss of hydrogen (aldehyde to carboxylic acid)



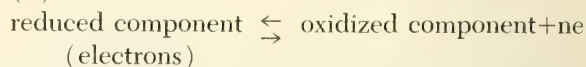
In reduction on the other hand there may be a loss of oxygen from a substance, or the addition of hydrogen, but fundamentally it is the gain of electrons by the substance being reduced that characterizes the reduction reaction. Since oxidation of one substance is invariably accompanied by reduction of another substance, an oxidation-reduction reaction implies a loss of electrons by the substance being oxidized and a gain in electrons by another substance able to accept electrons and undergo reduction. In living cells when molecular oxygen derived from the atmosphere is the ultimate hydrogen acceptor, the process is called respiration.

With the majority of known physiological metabolites, primary oxidation is actually accomplished by the removal of two hydrogen atoms, catalysed by specific cellular enzymes known as dehydrogenases. In a few instances the liberated hydrogen combines directly with molecular oxygen to form hydrogen peroxide and then water, but in the majority of cases the liberated hydrogen atoms or their electron equivalents are transported to molecular oxygen

by a series of reversible oxidation-reduction reactions. In the latter, oxygen appears only in the final stages of a chain of respiratory reactions, and then only in the form of water as the result of its reduction by hydrogen. In no known instance does oxygen combine directly with carbon to form carbon dioxide. Instead, carbon dioxide is extracted through the splitting out of carboxyl groups from metabolites by a process known as decarboxylation.

OXIDATION-REDUCTION SYSTEMS

An oxidation-reduction (O-R) system in simplest terms consists of two chemically related compounds which are capable of reversible transformation one into the other by the exchange of one or more electrons. For example, any O-R system can be represented as follows (3):



where (n) is the number of electrons transferred. The oxidizing or reducing power of such a system can be related to other similar O-R systems by comparison with a standard O-R system such as the hydrogen electrode. Adjustments are made for the fact that the hydrogen electrode is standardized at pH 0, whereas physiological systems must be measured at neutrality (pH 7). O-R systems with more negative potentials are more reducing than those with more positive potentials. For example, the hydrogen electrode with a potential of -0.421v at pH 7, represents a system with great reducing power, while the oxygen electrode with a potential of $+0.810\text{v}$ at pH 7 represents an opposite extreme of a system with great oxidizing intensity. O-R systems must be thermodynamically reversible so that a small change in the equilibrium of the solution must be able to convert one of the components into the other. The significance of O-R potential studies is that they provide a method of predicting the possibility of a reaction between two O-R systems, and that they give the sequence in which the systems will carry electrons. O-R potentials also predict the amount of free energy able to be released at a particular stage in a series of multiple O-R reactions. Dehydrogenases, co-enzymes, and cytochromes take part in cellular O-R systems, each with an O-R potential, and make possible cellular respiration.

A GENERAL OUTLINE OF CELLULAR OXIDATION

The chemical reactions found in cells obey the same thermodynamic principles that apply to chemical reactions found in inanimate systems. That is, the amount of energy liberated for comparable degrees of chemical change is the same in both cases. Theoretically when hydrogen combines with oxygen to form water, whether in the living cell or in an inanimate chemical reaction, the same amount of energy is released. In inanimate systems, this energy is liberated as free energy or heat and is lost. In the living cell, although a large portion of the energy liberated from the reaction is lost through dissipation of heat energy, a certain portion, perhaps a third or more, is stored as potential energy for use by the cell. The one significant difference between the animate and the inanimate system is that in cells, the union of hydrogen and oxygen is carried out at the end of a series of oxidation-reduction reactions, which is catalysed by a number of enzymes. At each step a fraction of the total energy of the basic reaction is released, and part of this energy is stored or taken up in the formation of new energy-absorbing compounds as chemical energy. Later as these compounds are broken down upon demand by the cell, the stored energy is released in approximately the same amount as was needed for synthesis of the compound.

It may be helpful at the onset to schematically represent the general outline of cellular oxidations. Taking first the cellular substance or substrate being oxidized, we see that these exogenous or endogenous protein, carbohydrate or fat molecules are first broken down by the removal of two atoms of hydrogen, a reaction catalysed by specific enzymes known as dehydrogenases. These reactions liberate energy which is either dissipated as heat, or is stored as chemical energy in new compounds usually as phosphate esters. As hydrogen is liberated it is carried away by a series of oxidation-reduction reactions, and is ultimately united

with molecular oxygen at the very end of the oxidation or respiratory series. Energy for cell work is stored at each step. Energy is similarly liberated and stored in the process of splitting off of carboxyl groups from certain compounds in the formation of carbon dioxide. Parenthetically it is of interest to note that the bulk of the oxidative systems apparently are found in the large granules (mitochondria) of the cell (4). A schematic diagram of oxidative metabolism (after Stanier (5)).

DEHYDROGENASES

The first chemical reaction in the liberation of energy from foodstuffs is the oxidation of the foodstuff or metabolite by the removal of hydrogen. This reaction is brought about by a specific cellular enzyme known as a dehydrogenase. Dehydrogenation can be accomplished by three methods:

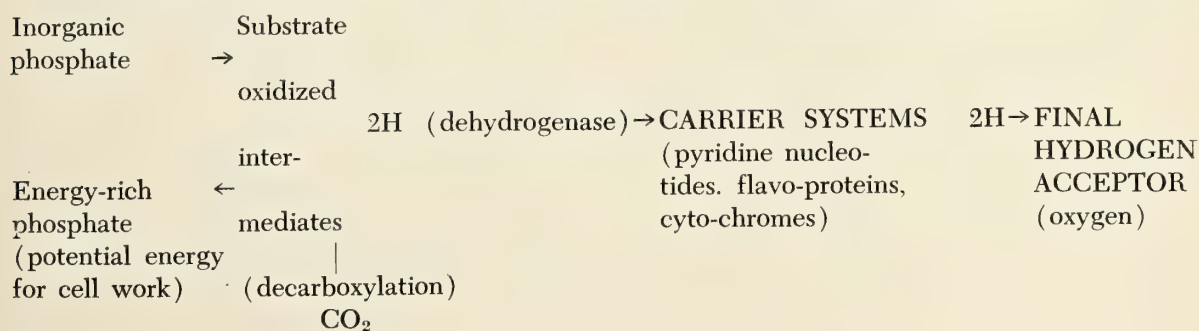
1. The direct transferal of hydrogen from the metabolite to molecular oxygen by a prosthetic group of the dehydrogenase protein so that peroxide is formed. The peroxide is then broken down into water by a catalase or a peroxidase, and the reaction is then complete. D-amino acid oxidase catalysing the dehydrogenation of certain flavoproteins is an example.

2. Hydrogen may be oxidized to water through the mediation of the cytochrome system, between a dehydrogenase system on one hand and molecular oxygen on the other.

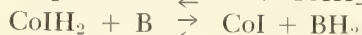
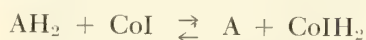
3. Hydrogen may be oxidized to water through the mediation of a complex series of oxidation-reduction systems including: dehydrogenase, codehydrogenase (coenzymes, pyridine nucleotides), flavoprotein, cytochrome, cytochrome oxidase, molecular oxygen. Most dehydrogenase systems are of this type.

COENZYME-LINKED DEHYDROGENASES

In aerobic dehydrogenase systems, the hydrogen liberated from cell metabolites is transferred in one direction toward molecular oxygen, so that the metabolite is oxidized by the removal



of hydrogen and hydrogen is oxidized by union with molecular oxygen. In anaerobic dehydrogenase systems, where oxygen is insufficient to meet the demands of the cell for energy, the hydrogen released may be oxidized by a hydrogen acceptor other than oxygen. A second dehydrogenase system with its own enzyme and substrate is linked to the first system by a specific coenzyme. Hydrogen is transferred and energy is stored without the immediate presence of molecular oxygen. Two coenzymes are known, coenzyme I or diphosphopyridine nucleotide (DPN), and coenzyme II or triphosphopyridine nucleotide (TPN), nicotinic acid amide being an essential component of each. Any coenzyme-linked reaction can be represented as follows:



where A and B are dehydrogenases acting as substrates and CoI is coenzyme I. At the moment of catalysis hydrogen is transferred from the substrate A to the coenzyme I. The reduced coenzyme I must be reoxidized immediately by a new hydrogen acceptor substrate B, in order that the linked dehydrogenase system may continue to react, for there is only a small amount of coenzyme present for reaction. Hydrogen transfer to molecular oxygen must be eventually carried out in order that chemical equilibrium be reached. Hydrogen may be transferred directly to molecular oxygen in a few cases, by way of another hydrogen accepting substrate, or in the case of most coenzyme-linked reactions in the respiratory series, by way of a specific flavoprotein, cytochrome, and finally molecular oxygen. A large number of dehydrogenases are associated with coenzymes, so that one coenzyme may react with a number of specific metabolites in the removal of hydrogen.

FLAVOPROTEIN

Flavoproteins are specific riboflavin-containing cellular enzymes that apparently catalyse the oxidation of coenzymes by cytochromes. A variety of these are found in bacteria, yeast, and other cells, in addition to those found in mammalian tissue. They are named, with the exception of the first-discovered "old yellow enzyme" of Warberg, according to the substrate and the manner in which they act. For example, cytochrome *c* reductase in yeast links the reduction of cytochrome *c* by coenzyme II.

Flavoproteins are believed to link the cytochromes with the dehydrogenase systems. Eleven flavoprotein enzymes are listed by Best and Taylor (3).

THE CYTOCHROME SYSTEM:

The cytochrome system functions at the extreme end of the respiratory chain of oxidation-reduction reactions, serving to make atmospheric oxygen available to the cell for oxidation of hydrogen which has been liberated from various cellular metabolites by the dehydrogenases at the beginning of the chain. The cytochrome system consists of a group of enzymes related to *heme* found in human hemoglobin. They are widely distributed in nature, being found in plants, certain aerobic bacteria, yeast, and also the muscle of vertebrates. Cytochrome *a*, *b*, *c*, and cytochrome oxidase are the found compounds that make up this system. Their chemical structure is that of a conjugated protein with an attached iron porphyrin or tetrapyrrol prosthetic group, resembling the tetrapyrrol structure of *heme* found in hemoglobin. Their structure also resembles that of chlorophyll found in green plants in which case magnesium replaces the iron atom in the tetrapyrrol structure. It is by means of this prosthetic group, or more specifically the iron atom contained in this prosthetic group, that the reversible oxidation-reduction reactions of cytochromes are possible.

Cytochromes and cytochrome oxidase, although closely related in their iron-porphyrin prosthetic groups are in other ways dissimilar. The cytochrome *oxidase* reacts with small amounts of cyanide to form a completely undissociable compound that inhibits electron transfer and paralyzes cellular respiration. Cytochromes *a*, *b*, and *c* do not react with cyanide. Carbon monoxide forms a similar undissociable compound with cytochrome *oxidase* that paralyzes respiration. In carbon monoxide poisoning, however, tissue poisoning does not occur because the gas first forms a non-dissociable compound with hemoglobin contained in erythrocytes and never reaches the tissues to poison the *oxidases*. Carbon monoxide does not react with cytochromes *a*, *b* or *c*. Finally, cytochromes *a*, *b* and *c* will not react directly with molecular oxygen, but are oxidized only through the mediation of cytochrome *oxidase*.

Fundamentally it is the iron atom of the prosthetic tetrapyrrol group that reversibly un-

Cytochromes a, b, or c	Cytochrome oxidase
1. Will not react with CN or CO.	1. Reacts with CN or CO to form undissociable compounds that completely inhibit electron transfer and paralyze tissue respiration.
2. Will not react directly with molecular oxygen.	2. Reacts directly with molecular oxygen at pH 7, in the presence of cytochrome.
3. Molecular weight 13,000.	3. Molecular weight 75,000.

dergoes oxidation or reduction and thus is able to effect electron transfer. Ferrous iron is seen to undergo oxidation to ferric iron with the loss of one electron, thus:

$$\overset{++}{\text{Fe}} \rightleftharpoons \overset{+++}{\text{Fe}} + e$$

Returning to the path of hydrogen transfer: Phosphopyridine nucleotide (DPN/TPN) transfers hydrogen to a fiboflavine di-nucleotide which in turn transfers hydrogen to cytochrome *b*. Hydrogen ions are furnished to the cytoplasm of the cell, while their electrons are forwarded through the cytochrome system in the order of cytochrome *b*, *c*, *a*, *oxidase*, and finally atmospheric oxygen. The hydrogen unites with oxygen to form hydrogen peroxide which is decomposed by the enzyme, catalase, to water and oxygen. Thus it is that the iron-containing cytochromes, functioning at the very end of the respiratory chain, carry out the final electron transfer of metabolic hydrogen to atmospheric oxygen, and in this way make available to the organism most of the oxygen that it consumes.

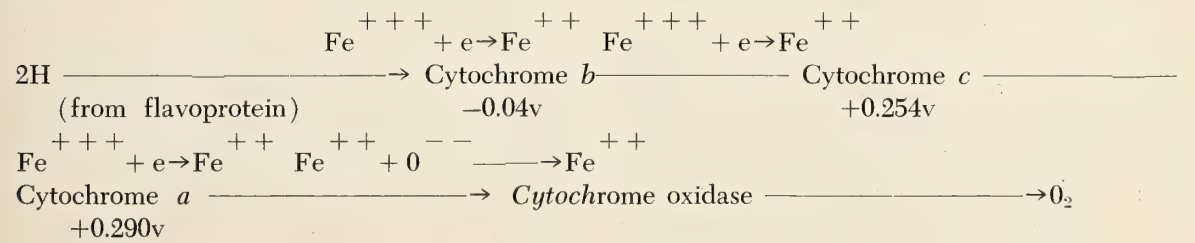
THE BIOLOGICAL COUPLING OF OXIDATION AND PHOSPHATE BOND ENERGY

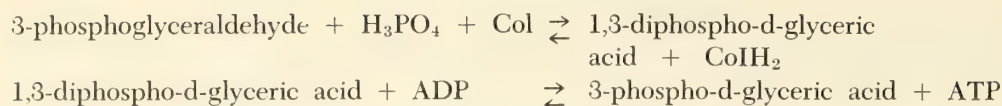
In preceding paragraphs we have seen how cellular oxidations have been effected by the removal of hydrogen from various cellular substrates. It must now be shown how the energy liberated by these dehydrogenations is used by the cell. It must further be shown how this energy is first stored and then released when called for by the cell to do its work.

The highest potential energy for cellular work has been found to be stored chemically in the "high-energy" phosphate bond. Ordinary "low

energy" phosphate ester bonds as typified in glycerophosphate involve a relatively small energy storage of 3,000 calories or less in their synthesis. The "low-energy" of this bond can be greatly increased by a simultaneous oxidation of glyceraldehyde to glyceric acid. Similar oxidative energy-liberating reactions occur in the glycolytic series, the Krebs cycle, and perhaps during the oxidation of lipids. The "high-energy" phosphate linkage represents a chemical compound with larger energy of formation and upon hydrolysis to inorganic phosphate results in the liberation of a quantity of energy comparable with that quantity that went into its formation. For example, at one stage of glycolysis (*vide infra*), inorganic phosphate is taken up by 3-phosphoglyceraldehyde, forming a hypothetical ester, 1,3-diphospho-glyceraldehyde. This compound is dehydrogenated by diphosphopyridine nucleotide (DPN) to 1,3-diphospho-glyceric acid. The change of molecular structure gives the phosphate bond in position *one* a great increase in potential energy. This phosphate radical is now transferred with its high energy content intact to adenosine-diphosphate (ADP), forming the 3rd phosphate group of adenosinetriphosphate (ATP).

Phosphate bond energy has been thus temporarily stored in ATP, ready for release to the cell upon demand, for muscle contractions, intestinal absorption, and other reactions. It has been computed that in the complete oxidation of each unit of glucose from glycogen by way of pyruvate, that 36 high energy phosphate bonds are accumulated and that 345,000 calories of heat energy are produced. Similar coupled





oxidation-phosphorylation reactions with the production of energy-rich phosphate linkages are not confined to mammalian tissues, but are also seen in the conversion of glycogen to glucose in yeast and in certain bacteria. One organism, *Thiobacillus thio-oxidans* is able to store energy-rich phosphate using the energy of sulfur oxidation carried out anaerobically and in the dark (to exclude photosynthesis as a source of energy).

CELLULAR RESPIRATION IN MUSCLE

One of the main uses to which the phosphate-bond energy stored in ATP is put is in muscle contraction. Muscle contraction is currently believed to be the shortening of partially unfolded polypeptid chains of actomyosin contained in the micellae of muscle myofibrils, a reaction set off by an electrical impulse or its chemical equivalent entering the muscle from its nerve. Two theories as to the contraction of actomyosin have been postulated. First, "energy-rich" phosphate from ATP passes to actomyosin at the time of stimulation, giving up its energy for work and heat, and leaving ADP plus inorganic phosphate. Second, "energy-rich" phosphate from ATP may pass to actomyosin previous to the muscle contraction, giving up its energy to partially unfold the polypeptid chain to a tensed state, so that it is ready to contract upon stimulation. The one theory regards the relaxed muscle with its extended actomyosin chain as a loose mechanism to be charged only upon stimulation, while the other theory regards the relaxed muscle as a bundle of taut, energy-charged, unfolded actomyosin chains, ready to shorten when nerve stimulation "pulls the trigger."

In either case, the fundamental chemical event in the contraction is the splitting of adenosinetriphosphate (ATP) by an enzyme adenosinetriphosphatase (ATPase), activated by calcium ions before or during the initial anaerobic phase of muscle contraction. As the result of its action, one of the energy-rich phosphate bonds is passed from ATP to actomyosin leaving adenosinediphosphate (ADP). The ADP does not react further with actomyosin. When actomyosin contracts, the energy of the attached phosphate bond is spent. Phosphate is released

as inorganic phosphate which may be reused in the phosphorylation of carbohydrate compounds. High energy phosphate bonds may thus be found in three compounds, actomyosin phosphate, adenosinetriphosphate, and creatine phosphate. The creatine phosphate can be compared to a bank, storing "energy-rich" phosphate bonds instead of money, for use by muscle. Like a bank it needs a teller, in this case ATP, to distribute this energy on demand.

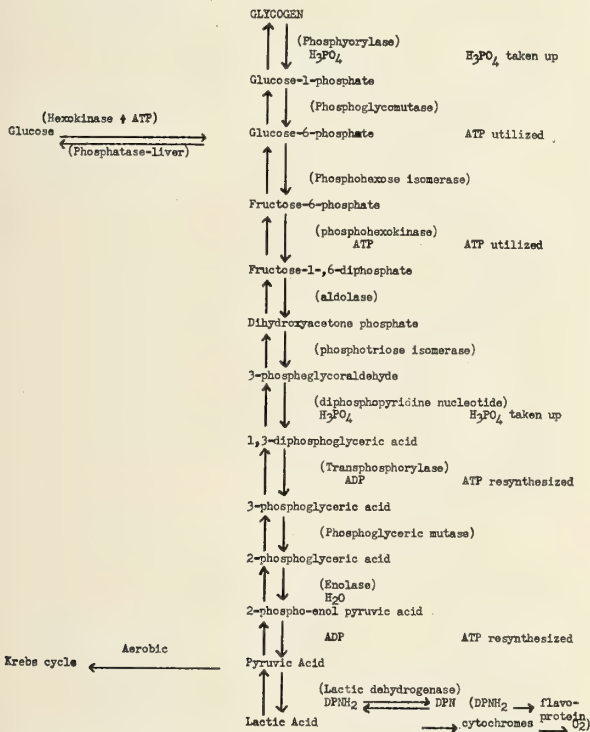
Later in the muscle recovery or aerobic phase, phosphate bonds are generated by glycolysis for transfer to the above compounds. Glycogen catalysed by phosphorylase at the beginning of contraction takes up inorganic phosphate (H_3PO_4) and simultaneously splits off glucose-1-phosphate. There then begins a series of complex anaerobic transformations of glucose-1-phosphate to its degradation product of pyruvic acid with a production of 29,000 calories of energy. It is at this final stage of glycolysis that we can begin to see some connection between muscle work and more direct oxidation-reduction systems previously discussed. To repeat, under the initial anaerobic phase of muscle contraction, or in periods of sustained contraction and oxygen debt, glycolysis proceeds to the pyruvic acid stage, and this pyruvic acid is eventually converted to carbon dioxide and water with the production of energy and heat. This energy is used for the resynthesis of phosphocreatine and ATP. Pyruvic acid may be reversibly reduced to lactic acid under anaerobic conditions, as in severe exercise. If oxygen then becomes available as it normally would at the conclusion of muscle contraction, the reduced coenzyme (DPNH_2) gives up its hydrogen not to pyruvic acid, but to molecular oxygen through a specific flavoprotein (riboflavin di-nucleotide) and the cytochrome system. As a result, no lactic acid need be formed under aerobic conditions, glycolysis ending at the pyruvic acid stage. As to the disposal of this pyruvic acid, we may note that in the presence of oxygen, pyruvic acid is oxidized via oxaloacetic acid in the well-known Krebs or tricarboxylic acid cycle. The net result of this Krebs cycle is the formation of three molecules of carbon dioxide, two molecules of water, and one mole-

cule of oxaloacetic acid which is reused time and again. In this process, some 325,000 calories are liberated for use chiefly in the resynthesis of glycogen from lactic acid.

The energy made available to the cell for muscular work is summarized in the chart below(3):

Reaction	Purpose	Calories Released
ATP → PC + ADP	Energy for muscle contraction	12,000
CP + ADP → C + ATP	Energy for resynthesis of ATP	10,000
Glycogen to lactic acid (Glycolysis)	Energy for resynthesis of phosphocreatine and ATP	29,000
Oxidation of lactic acid (Tricarboxylic acid cycle)	Energy for resynthesis of glycogen	325,000

ANAEROBIC GLYCOLYTIC CYCLE OF MUSCLE



TRICARBOXYLIC ACID CYCLE (KREBS)

In the Krebs cycle a molecule of the 6-carbon compound, tricarboxylic acid or *cis*-aconitic acid is formed by the condensation of one molecule each of pyruvic and oxaloacetic acids, with the release of a molecule of carbon dioxide. *Cis*-aconitic acid is hydrated to form isocitric acid, which is in equilibrium with citric acid, the latter possibly acting as the governor of the over-all speed of reaction of the Krebs cycle. Isocitric acid is oxidized in turn to oxalosuccinic acid. The latter undergoes decarboxylation with the production of the 5-carbon di-carboxylic acid, a-ketoglutaric acid, with the release of another molecule of carbon dioxide. Further

oxidation results in the formation of the 4-carbon succinic acid and the release of the 3rd and final molecule of carbon dioxide from the original pyruvic acid. Succinic acid is oxidized through fumaric and malic acids to oxaloacetic acid, and the cycle then repeats. At each turn of the cycle, each molecule of pyruvic acid

which enters, yields two molecules of water and three molecules of carbon dioxide, while a molecule of oxaloacetic is reformed. A single molecule of oxaloacetic acid can be used in this way repeatedly in the oxidation of pyruvic acid to carbon dioxide and water; it therefore acts in the manner of a catalyst.

The above reactions producing carbon dioxide require diphosphothiamine as a coenzyme (co-carboxylase) and the various oxidations mentioned are accomplished by specific dehydrogenases, employing phosphopyridine nucleotide or riboflavine nucleotides as coenzymes.

Pyruvic acid is in equilibrium with members of the tricarboxylic acid cycle. This cycle is probably the final common path for much of the carbohydrate, fat and protein metabolism. Its reactions liberate energy, and most of this energy is used for the establishment of energy-rich phosphate bonds.

CARBON DIOXIDE FIXATION

Not all carbon dioxide liberated in the course of catabolism is excreted, but a certain portion is utilized by the tissues for the synthesis of complex carbon containing compounds such as glycogen. Carbon dioxide utilization or *fixation* is possible by two known mechanisms. First of all Werkman and Wood(6) have postulated that glycogen can be formed by the condensation of pyruvic acid and carbon dioxide. Hastings et al(7), using carbon dioxide containing radioactive carbon (C¹¹) have shown in rats that carbon dioxide is incorporated into liver glycogen laid down when lactic acid is fed, presumably from pyruvic acid condensation with carbon dioxide. Carbon dioxide fixation also occurs in the isocitric acid, a-keto-glutaric acid and succinic acid reactions of the Krebs cycle.

In this way it is possible for cells to take a 2-carbon or 3-carbon compound, and by successive addition of carbon dioxide, synthesize a 6-carbon compound. It has been further demonstrated that carbon dioxide is fixed not only in carbohydrate derivatives by muscle, but also in certain nitrogenous compounds, probably amino acids.

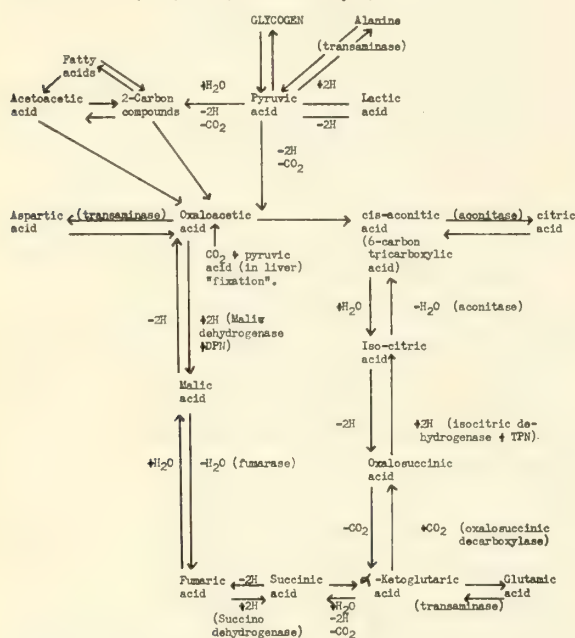
The discovery that carbon dioxide is utilized (fixed) by animal cells as well as plant cells is an important one, for it changes our concept that carbon dioxide is merely a cell waste product. It might be pointed out that the only difference between plant and animal utilization of carbon dioxide, is that the energy for this utilization in animals is derived from the oxidation of foodstuffs, while in plants it is the consequence of the photosynthetic energy of the sun on chlorophyll.

their clinical action and the site of their chemical effect on cellular respirations is known. Current research is constantly enlarging our knowledge of these cellular oxidations, and we can expect a much more complete understanding of these biological processes within our own lifetime. Only a few of the clinical applications of these investigations will be mentioned now.

An accumulation of tissue metabolites or an elevation of the body temperature is known to increase the metabolic rate of the organism, and this effect has been ascribed to the acceleration of the cytochrome system reactions. Cytochromes are activated by a high concentration of atmospheric (molecular) oxygen so that higher oxidizing potential would be available to them in an atmosphere of pure oxygen. This puts oxygen therapy on a firm theoretical, instead of an empirical basis. Knowledge of the site of cellular molecular oxygen utilization, however, enables us to define the limitations of oxygen therapy, for any factor which would prevent oxygen from reaching the tissues (anemia, decreased blood volume, pulmonary disease, circulatory failure, carbon monoxide poisoning of hemoglobin carried in erythrocytes) or which would prevent the oxidation of the cytochromes themselves (e.g. cyanide, sulphide, nitrite poisoning) would inhibit the remaining cellular oxidations.

Cyanide poisoning. In this connection we have seen how the cyanide ion completely inhibits electron transfer in the cytochrome system by immobilizing cytochrome oxidase. Poisoning from the accidental or intentional use of hydrocyanic acid gas or compounds able to release cyanide ion in the body causes asphyxia despite full oxygen saturation of the blood. Indeed at autopsy of fatal cases of cyanide poisoning, the blood is found to be bright red due to its high oxygen content. Death from tissue asphyxiation occurs in 95 per cent of cases within a few minutes, but in certain instances treatment can be effectively administered if begun promptly. Methemoglobin effectively competes with the cytochromes for the cyanide ion, and forms a stable cyanhemoglobin which is then excreted. Prompt administration of amyl nitrite by inhalation or 1 per cent sodium nitrite or methylene blue intravenously will cause the production of methemoglobin which then unites with the cyanide ion, freeing the cyto-

TRICARBOXYLIC ACID (KREBS) CYCLE (after Best and Taylor)



CLINICAL ASPECTS TO THE PHYSIOLOGY OF CELLULAR RESPIRATION

Since cellular respiration begins with almost the first chemical reactions within the cell, and involves the breakdown of all endogenous and exogenous foodstuffs, almost any factor which would affect cellular respiration would affect the total cell metabolism. Perhaps all of the drugs, chemicals, antibiotics and even toxic agents with which we are familiar have their effect by modifying cell metabolism through cellular respirations. Certain of these substances have been investigated so that the basis of

chromes, and saving the patient.

Diphtheria toxin has recently been thought to in some way immobilize cytochrome *b*, and thus exert its toxic effect.

Cytochromes intravenously. It might be well to ask why supplemental cytochromes could not be given in instances where poor tissue oxygenation might be expected. Cytochrome *c* is the only cytochrome that has been obtained in pure form so far, and it has been given to subjects in which artificially induced anoxia produced abnormal EKG tracings. 50-60 mgm of cytochrome *c* given intravenously was found to revert these EKG tracings to normal, although the authors(8) doubted the ability of the enzyme to enhance the myocardial utilization of oxygen. Other authors(9) found that 50 mgm of cytochrome *c* given intravenously had no ability to increase the capacity for effort without pain of patients with angina of effort over that effect produced by placebos.

Alkaloids and Anaesthetic Agents. Turning to the opposite end of the respiratory chain, it is now believed that alkaloids and probably most anaesthetic agents have their depressant action on tissue dehydrogenases. This would suggest that in the administration of certain anaesthetics, while one end of the respiratory chain is selectively depressed, that the other end should be fully activated. The generous use of oxygen during anaesthesia in order to fully oxygenate the cytochrome system seems justified.

The Role of Vitamins in Intracellular oxidations. Certain vitamins are essential to the formation of hydrogen carriers in the intermediate portion of the respiratory chain. Nicotinic acid in the form of its amide is required for the formation of coenzyme I and II (the pyridine nucleotides). Riboflavin is required for the formation of (ribo) flavine nucleotides. Pyridoxine (B-6) has recently been discovered to be essential in transamination, in which amino groups are transferred from one compound to another. Pantothenic acid is known to be involved in certain acetylations, and vitamin B-12 has been discovered to speed the conversion of purine in nucleoprotein to uric acid by xanthine oxidase. A good dietary regimen, adequate in these vitamin factors probably insures the proper function of these phases of respiration, especially in times of stress, such as in the acute depression of one part of the respiratory chain by an anaesthetic or toxic agent. Vitamin

B-1 in the form of diphosphothiamine is an essential part of the coenzyme, cocarboxylase, which makes possible the catalysis of carboxylic acid to carbon dioxide. This reaction is the only important source of carbon dioxide of metabolic origin. Cocarboxylase also helps in the resynthesis of glycogen from carbon dioxide, and is thus necessary for carbon dioxide fixation.

The Role of Hormones in Intracellular Respirations. It is now felt that all hormones have some effect in influencing the rate of certain of the respiratory reactions. From work done by Cori et al (10 and 11) it was discovered that hexokinase in the liver catalysed the phosphorylation of glucose by ATP to glucose-6-phosphate and that this reaction was inhibited by the diabetogenic hormone of the anterior pituitary, reinforced by a hormone from the adrenal cortex. Insulin was found to remove this inhibition. The question of the effect of thyroid hormone on the exchange of liver ATP in these phosphorylations has not been settled by radioactive isotope studies(12).

At least one of the adrenal cortical steroids, desoxycorticosterone, has been found to inhibit D-amino acid oxidase(22).

Undoubtedly many drugs have their action dependent on alteration of the respiratory enzymes or their rates of reaction. Only one of these will be mentioned because of its recent clinical interest. Tetraethylthiuran disulfide ("Antabuse") is a compound without pharmacological action in itself. When alcohol is taken following antabuse ingestion, there occurs an uncomfortable clinical reaction consisting of nausea, vomiting, generalized vasodilatation, correlated with an increase in blood acetaldehyde. These same symptoms can be reproduced by the administration of acetaldehyde. It has been postulated that antabuse inhibits xanthine oxidase, one of the cellular dehydrogenase systems capable of oxidizing acetaldehyde, thus causing an accumulation of acetaldehyde in the blood(13).

SUMMARY

Cellular respiration has been discussed from the point of view that it consists of all those biochemical reactions, usually oxidations, that convert bound energy in foodstuffs into free energy for cell use. The manner in which these oxidations have been effected through the removal of hydrogen and carbon dioxide has been detailed, and methods by which the cell stores

this free energy at higher energy potentials has been indicated. Finally certain clinical aspects of the physiology of cellular respiration have been briefly mentioned.

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PHOENIX *Clinical* CLUB

MASSACHUSETTS GENERAL HOSPITAL CASE NO. 29462

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

An eighteen-year-old boy was first seen in the Out Patient Department, about one year before the present admission because of hemoptysis of four years' duration.

At the age of thirteen, while playing, he coughed up several large clots of blood. He had a similar episode one week later, and there were repeated intermittently up to the day of his visit to the Out Patient Department. The amounts raised varied from a speck to half a cupful. No definite statement was made concerning the frequency of attacks, but "at no time were they more than two weeks apart." There were no chills, fever, night sweats or chest pain until "recently," when he had noted sharp twinges of pain in the right upper chest unassociated with cough or hemoptysis. There had been no history of inhalation of foreign body, antecedent upper respiratory infection, known contact with tuberculosis or undue bleeding tendency. He had fractured the left collar bone one year before onset of his symptoms, he was in a cast for two months.

Examination in the Out Patient Department showed a well-developed and well-nourished boy in no distress. The chest was well developed. There was dullness over the right upper lobe posteriorly to the midscapular region and anteriorly to the fourth rib, with occasional expiratory bubbling and coarse crepitant rales posteriorly. Kronig's isthmus was slightly narrowed on the right. The lungs were otherwise clear. The heart was in its usual position and normal in size. The abdomen was negative. There was no clubbing of the fingers.

The blood pressure was 138 systolic, 68 diastolic. The temperature was 98°F., the pulse 60, and the respirations 20.

X-ray examination of the chest showed a round, homogeneous soft-tissue mass in the upper posterior mediastinum measuring approximately 11.5 cm. in diameter, without any evidence of calcification or cavity formation. The tumor obliterated the upper portion of the right lung but the visible portion of the right lung and the left lung appeared clear. The hilar shadows were normal and equal on both sides. The heart was not remarkable. No definite bone involvement could be seen, but there was a questionable pressure defect on the right lateral aspect of the fourth dorsal vertebra, with narrowing of the right pedicle. The trachea appeared straight in the midline and there was no mediastinal displacement. No fluid was present. Bucky films of the chest confirmed the

presence of the large mass in the lung. An area of probable slight erosion of the upper aspect of the sixth rib was also seen. There was an irregular air pattern in the region of the mass, probably due to partially collapsed lung that was superimposed on the shadow of the mass.

While being followed in the Out Patient Department, the patient developed wheezing, especially at night. No other information was given regarding these attacks except that "he was quite free of wheezes at times." He was free of pain and maintained his weight. Bronchoscopy showed "extrinsic pressure but failed to reveal the source of the bleeding, although a moderate amount of bright-red blood was seen in the trachea and right main bronchus." Hospitalization was advised but refused.

For the next ten months he remained free from pain, hemoptysis and cough. At the end of this period he obtained a job in a weaving mill, doing heavy labor. Eight days before entry he suddenly became dyspneic while working. The dyspnea forced him to leave his work. Six days prior to admission he developed severe pain in the right anterior chest and he was admitted to a community hospital, where x-ray films showed a lobulated tumor mass in the upper half of the right lung, with pleural effusion. Two chest taps yielded 100 and 300 c.c of reddish-brown pleural fluid and gave considerable relief. He was transferred to this hospital.

Physical examination showed a poorly nourished, cyanotic and dyspneic man with anxious, pale facies and visible flaring of the alae nasi on breathing. The right chest was splinted during inspiration. There were dullness and diminished tactile fremitus and breath sounds over the right upper and lower lobes. Dullness was obtained over the right middle lobe, with egophony and increased tactile fremitus. Pectoriloquy was heard over the right upper lobe posteriorly and over the middle lobe anteriorly. The diaphragmatic excursion was poor on the right. The heart was normal. The remainder of the examination was not remarkable.

The blood pressure was 130 systolic, 60 diastolic. The temperature was 99.6°F., the pulse 128, and the respirations 25.

Examination of the blood showed a red-cell count of 4,100,000, with 75 per cent hemoglobin. The white-cell count was 11,000 with 89 per

cent neutrophils. A blood Hinton test was negative. The prothrombin time was 28 seconds (normal 16 seconds); the hematocrit was 39.2 per cent. The nonprotein nitrogen was 10 mg. per 100 c.c., and the protein 5 gm. The van den Bergh test was normal. Urinalysis was negative.

X-ray examination of the chest, almost a year after the first one, showed the tumor mass still present. The right pleural cavity was filled with a fairly large amount of fluid and there was partial collapse of the right middle and lower lobes, which had a honeycombed appearance. The left lung appeared clear, but there was questionable crowding of the markings in the left lower lobe.

During the next ten days, three chest taps yielded 2800, 1500 and 1000 c.c. of dark bloody fluid, which on smear and culture was negative for organisms. No tumor cells were seen in the sediment.

Repeated x-ray studies after the taps showed that, instead of a fluid level, there was an area of increased density with irregular markings extending along the lateral axillary line. There were numerous irregular areas of decreased density in the right upper chest, either in the tumor or in the pleural cavity. None of the visualized bones, especially the ribs, showed evidence of destruction and no other changes were noted. Another bronchoscopy, year after the first, was negative. No evidence of intrinsic or extrinsic tumor was seen.

On the eleventh hospital day an operation was performed.

DR. LOUIS B. BALDWIN:

The outstanding features of this case are the long duration of the illness with frequent hemoptysis but without other symptoms until about five years after the onset, and the period of ten months when there was no chest pain, no hemoptysis and no cough. Following this period however there was the acute advent of marked dyspnoea and the rapid reaccumulation of bloody pleural fluids.

When first seen in the out-patient department he had been coughing up blood frequently for four years. He was in good general physical condition, but the physical signs pointed to a lesion in the right upper chest. A detailed x-ray report, at this time, indicated that there was a homogeneous tissue mass in the upper posterior mediastinum, without evidence of calci-

fication or cavity formation. The hilar shadows were normal and equal on both sides. Bronchoscopy showed extrinsic pressure but failed to reveal the source of the bleeding.

In spite of the thorough roentgenological studies we are still in some doubt at this point whether we are dealing with a tumor originating in the mediastinum, in the pleura, or in the lung, or in the bony framework of the chest. It would be hard to conceive of a tumor in the posterior mediastinum producing early hemoptysis and it would be equally difficult to picture a tumor of the pleura with invasion of the lung, remaining silent except for moderate chest pain and hemoptysis for so long a time. If we can put any reliance on the protocol it is inconceivable that we are dealing with a bronchogenic carcinoma, not only because of the age of the patient, and the description of the mass but also because of its subsequent course.

A tumor originating in the bony framework such as osteosarcoma can be readily ruled out by the repeated x-ray studies which revealed no bony involvement. Primary neoplasm of the pleura must be seriously considered in spite of the fact that they are rare. They may be benign or malignant originating in either the subserous layer or the surface of the pleura. These tumors may be localized or diffuse. Golden states that localized pleural neoplasms may exist as pedunculated masses and are generally fibrosarcomas of low malignancy.

By x-ray they appear sharply demarcated, rounded or oval, and may or may not show a lobulated border. They are very difficult to differentiate from a primary carcinoma of the lung. They grow slowly, sometimes existing for many years. Eventually, unless they metastasize they fill the pleural cavity and cause death by interfering with pulmonary circulation.

So call endotheliomas or mesotheliomas have their origin in the surface lining of the pleura. They may also appear by x-ray as a rounded, sharply demarcated mass. These tumors may be slow growing and tend to infiltrate the outer zone of the lung, dipping into interlober fissures. As a rule, carcinomas associated with massive pleural involvement metastasize late in the disease. Rubin states that sooner or later neoplasms of the pleura usually cause massive sero-hemorrhagic effusions which rapidly reaccumulate in spite of repeated chest aspirations.

If this patient has a tumor of the pleura it cannot be the non-invasive benign tumor such as fibroma, lipoma, and chondroma.

How does the consideration of a pleural mesothelioma fit this case?

To be sure the duration of five years or longer makes the diagnosis questionable; for these tumors rarely last more than two years before invading the pericardium and the diaphragmatic and mediastinal reflections of the pleura. They may extend to involve other organs and tissues. It is also difficult to conceive of a mesothelioma causing hemoptysis for four years or longer without other symptoms.

The same objection may be made in the consideration of a fibrosarcoma of the pleura, moreover these tumors rarely, if ever, invade the lung to produce hemoptysis.

But whatever the primary condition characterized by an upper right chest mass and hemoptysis the later developments and x-ray studies indicate extensive pleural involvement with a bloody pleural fluid and an area of increased density with irregular markings extending along the lateral axillary line. It is to be noted that malignant neoplasms of the lung and pleura are the cause of from 65 to 85 percent of hemorrhagic pleural effusions. In Berliner's material consisting of 120 cases, tumor cells were found in 50% of the hemorrhagic fluids complicating malignant neoplasms. The failure to find tumor cells in the present instance therefore does not prove that malignancy is ruled out.

Hemorrhagic pleural effusions are common in pulmonary infarction and infrequent in tuberculosis. They may be due to local circulatory disturbances, such as pressure exerted by an aortic aneurism or tumor on a large intrathoracic vein. Tumors in the anterior mediastinum are more likely to produce this condition, such as thymic tumors or teratoid tumors. Harrington cites an instance of a benign tumor associated with a bloody effusion.

Next in importance diagnostically are the mediastinal tumors. The lymphomas such as Hodgkins disease and lymphosarcoma are often first detected in the mediastinal lymph nodes. The former is more common in youth and roentgenologically is characterized by enlarged discrete hilar nodes extending laterally from the mediastinum, usually bilaterally. They are either sharply circumscribed or lobulated or fus-

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Actions and Uses.—Methantheline bromide, a parasympatholytic agent, produces both the peripheral action of anticholinergic drugs such as atropine and the ganglionic blocking action of drugs such as tetraethylammonium chloride. Tolerated amounts of methantheline bromide exert side effects typical of atropine-like drugs, but cause less tachycardia, and also less postural hypotension than does tetraethylammonium chloride. Toxic doses produce a curare-like action at the somatic neuromuscular junction.

Clinical studies indicate that the drug effectively inhibits motility of the gastrointestinal and genitourinary tracts and, to a variable degree, diminishes the volume of perspiration and salivary, gastric and pancreatic secretions. It also decreases mucoprotein secretion. Like atropine, it produces mydriasis and cycloplegia when applied locally to the eye or administered systemically, but until more clinical evidence becomes available, its local use for this purpose is not recommended. The value of the drug for preventing abnormal cardiac reflexes through the vagus during thoracic surgery, or as an agent for routine preoperative medication in place of atropine, requires further investigation before final conclusions can be reached.

Methantheline bromide is indicated for clinical use whenever anticholinergic spasmolytic action is desired, provided it is not contraindicated because of its atropine-like characteristics or because of a patient's intolerance to the unavoidable side effects of such therapy. It is useful as an adjunct in the management of peptic ulcer, chronic hypertrophic gastritis, certain less specific forms of gastritis, pylorospasm, hyperemesis gravidarum, biliary dyskinesia, acute and chronic pancreatitis, hypermotility of the small intestine not associated with organic change, ileostomies, spastic colon (mucous colitis, irritable bowel), diverticulitis, ureteral and urinary bladder spasm, hyperhidrosis or control of normal sweating which aggravates certain dermatoses, and control of salivation.

Methantheline bromide produces some degree of cycloplegia and mydriasis in therapeutic doses and

therefore should not be administered to patients with glaucoma. It sometimes decreases the ability to read fine print. Xerostomia (dryness of the mouth) is a common, sometimes transient, side effect. Urinary retention of varying degree may occur in elderly male patients with prostatic hypertrophy, and some patients may have difficulty emptying the rectum. Patients with edematous duodenal ulceration may experience nausea and vomiting during initial administration of the drug. These patients should take only liquids during the institution of drug therapy. All patients should be advised of the possible occurrence of side effects. Overdosage sufficient to produce a curare-like action may be counteracted by prompt subcutaneous injection of 2 mg. of neostigmine methylsulfate.

Dosage.—Methantheline bromide is administered orally or parenterally by either the intramuscular or intravenous route. Parenteral administration is not advised for patients able to take the drug orally. The average initial adult dose, oral or parenteral, is 50 mg. For patients with considerable intolerance, 25 mg. may be employed. In the management of peptic ulcer, a beginning schedule of 50 mg. three times daily before meals and 100 to 150 mg. on retiring is suggested. However, the usual effective dose is 100 mg. four times daily, although some patients may require more or less than this amount. The dosage may be increased to tolerance, using dryness of the mouth as a guide, and adjusted to meet the individual response of patients. Maintenance dosage in peptic ulcer is usually considered to be about one-half the therapeutic level. In the management of other hypermotile or hypersecretory states, the dosage should be adjusted to the smallest amount which will relieve the symptoms. When spastic conditions are secondary to inflammatory or other organic lesions, therapy directed toward the cause should be employed whenever possible.

G. D. SEARLE & CO.

Tablets Banthine Bromide: 50 mg.

Ampuls Banthine Bromide: 50 mg.

ed into large masses. A delicate reticulation is often seen extending into the adjacent lung tissue. There is seldom intrathoracic displacement. There may be widening of the right mediastinal shadow extending to the root of the neck but unlike the description in this case the borders are straight. The lungs are involved in 13 percent and the pleura in 11 percent in 214 cases studied by Pierce, Jacox, and Hildreth. Moulten found pleural involvement in 9 of 18 cases of Hodgkins. The fluid may be serous, chylous, or even bloody. The majority of the pleural lesions consist of scattered nodules or flat infiltrations. But extensive indurations involving also the ribs and spine are not uncommon. Radiotherapy is effective even if the pleura contains considerable fluid. When the lung is involved there may be hemoptysis.

Surely Hodgkins disease or lymphosarcoma in this case could have been easily ruled out by the use of radio-therapy. Mediastinitis and sarcoidosis may be mentioned in passing but are obviously not involved in this case.

Of the mediastinal tumors there are those of the anterior and posterior mediastinum. Among the former are the teratoid tumors which are usually cystic structures. They often contain all types of tissues, not only undifferentiated cellular elements, but also rudimentary organs. Solid tumors are less frequent and more liable to undergo malignant changes. The fact that in the present instance the mass is described as being in the posterior mediastinum rules out this diagnosis. For the same reason thymic tumors and intrathoracic thyroid are ruled out.

In the posterior mediastinum are found the neurogenic tumors. They arise from the spinal, intercostal, and sympathetic nerves and ganglia. Kent and his co-workers found only two instances of neurogenic tumors in the anterior mediastinum. These tumors have been found accidentally in the course of routine roentgen examinations. If symptoms are present, their nature depends on the size of the tumor, the nerves involved, the presence of malignant changes. Pressure may produce a Horner's syndrome or hoarseness. By roentgenology areas of calcification may be seen. A diagnostic pneumothorax reveals the tumor to be extra pulmonary. Lobulation of the tumor is suggestive of malignancy. Erosion of ribs or vertebral bodies may be caused by pressure alone.

It is difficult to conceive of a neurogenic tumor

causing hemoptysis for five years without there being metastatic lung involvement. It is however possible that enough pressure was exerted by the growth on the lung to produce changes in the lung or smaller bronchial tubes, or there might have been actual invasion of the lung by the growth. Tumors such as bronchogenic cysts and cystic hygromas do not produce the clinical picture seen in our case. There are other rare tumors however which may occur in the posterior mediastinum such as fibrosarcomas or myxosarcomas.

It is obvious that our patient does not have a bronchogenic carcinoma. His age and the course of the illness are against this diagnosis. But he might have a bronchial adenoma. These tumors arise in the bronchial mucus glands or in their ducts. They are either globular or pedunculated. They often originate within the bronchial wall and extend into the peribronchial tissue. A few instances have been reported with regional and even distant metastases. Adenomas usually occur in young individuals. The tumor chiefly affects females and predominantly the left lung. The outstanding symptom is recurring hemoptysis. The physical and roentgen findings are not unlike those encountered in bronchogenic carcinoma. These tumors usually remain within the lung but rarely they may extend into the mediastinum. I do not feel that this patient had a bronchial adenoma.

In conclusion we have an 18 year old boy who for years has had a mass in the upper posterior mediastinum without evidence of lung involvement, except for a few rales heard at the right apex and attacks of wheezing, which might be explained by pressure of the mass on the lung. There were no constant changes noted in the ribs and vertebrae in serial studies, but there was a prolonged history of hemoptysis, and the sudden final breakdown occurred after a period of heavy work. The later x-rays showed the same mass presumably unchanged in size but with an area of increased density along the lateral axillary line. This is interpreted as showing evidence of pleural metastasis but the meaning of the other findings is not clear, unless the areas of decreased density in either the pleural cavity or the tumor are further evidences of malignant changes. We have no evidence of a distant metastatic focus such as a testicular teratoma or a renal hypernephroma.

My first choice in diagnosis is, Mesothelioma of pleura; (2) Neurogenic tumor of mediastinum; (3) Bronchial adenoma (very unlikely)

DIFFERENTIAL DIAGNOSIS

Dr. Austin Brues: I should like to discuss this case mainly from the standpoint of its natural history, which seems rather specific and characteristic. The boy had a lesion that had apparently existed for at least five years and first gave symptoms at the age of thirteen. The history divides itself in to three phases. First, there was a long period in which the only symptom was rather persistent hemoptysis. Secondly, after four or more years there was a period of wheezing, suggesting bronchial compression. Finally, there was an acute sudden episode with pain in the anterior chest and dyspnea, and the rapid development of bloody pleural effusion. To this history we can add the finding of a round mass inside the chest, apparently arising from the posterior mediastinum, and presumably the seat of the symptoms. We have no evidence of disease elsewhere in the body, except that he had a prolonged prothrombin time and a low serum protein, however, the van den Bergh test was normal, and we have insufficient evidence to implicate the liver.

The question that we have to settle is, What sort of isolated mass in this location will progress to give this sort of history? Obviously this was not an acute infectious process. It might for hemoptysis, and there was no evidence of the bronchial nodes or to tuberculosis arising from the spine. The entire early course of the process, however, was essentially silent except for hemoptysis, and there was no evidence of infection or tuberculosis elsewhere. I consider that an infectious process of any sort is unlikely. A hydatid cyst of the mediastinum, first giving rupture into the bronchus, later into the pleural cavity, might give rise to this sequence of symptoms; but we have no reason to suspect an unusual environmental association and the patient had no eosinophilia. Moreover, no eosinophilia was noted even after extension of the process into the pleural cavity, which, if due to rupture of a hydatid cyst, would have caused a certain amount of the cyst contents to be absorbed.

In a young patient we must think of a congenital anomaly-bronchostenosis or a lung cyst. A condition of this sort would most likely

progress to serious symptoms only if it became secondarily infected. Again I point out that infection was not a perceptible element in the clinical picture.

This brings me to tumor. The long duration is in favor of a benign tumor or a tumor that underwent malignant change late, that is, during the last year. Lymphoma can exist for a period of many years without characteristic progression. Such a lymphoma would be the giant follicular type or a very scirrhus type of Hodgkin's disease. I should point out that hemoptysis is a rare symptom in lymphoma, and if it does occur it suggests that one is dealing with a particularly invasive form, which would not be the type giving a long, relatively quiescent history. It seems to me the presumptive diagnosis is a teratoma, not well enough differentiated, as is the classic dermoid cyst, to show calcification by x-ray or to yield hairs or other recognizable elements in the sputum or pleural fluid. The life history of this process is emphatically in favor of this diagnosis. These tumors appear early in life, may give their first symptoms at puberty or later, and sometimes give hemoptysis over a long period. Eventually they are likely to undergo malignant change or to rupture. I should be in favor of rupture as the explanation of the final episode here because of the extreme acuteness of its onset, although invasion of the pleura is a possible explanation, and would point to malignant change. I do not believe that it is necessary to assume, however, that the process had become malignant.

The fly in the ointment is the location of the lesion. It was apparently posterior in position, whereas dermoid cysts and teratoid tumors are almost always found in the anterior mediastinum.

Typical neoplasms of the posterior mediastinum are of neural origin. The history, however, is against one of these. They grow behind the pleura, and one would not expect cough and hemoptysis to be the earliest symptoms. Because of their location they frequently produce Horner's syndrome or pain early in the course of their development. The first symptom here was hemoptysis, which suggests that the lesion was near the bronchi and not posterior to the pleura. There are various rare tumors, such as chondroma, endothelioma, angioma and lipoma, that might arise in this location. There is one

thing somewhat in favor of the possibility of an angiomatous tumor—the characteristic picture of bleeding with which the history started.

I wonder if we might see the x-ray films.

Dr. Laurence L. Robbins: These films show a fairly smooth mass arising posteriorly in the mediastinum, or apparently arising in the mediastinum. The one thing in favor of the neural type of tumor, in addition to its location posteriorly, is that there is a definite erosion of the pedicle of the fourth thoracic vertebra. So far as the ribs are concerned, I am not at all sure that there are any definite changes. This is the shadow described as an irregular area overlying the mass and representing aerated lung. I am not convinced of that. The only other possibility is that it is fat within the tumor. It is difficult to be sure, and most likely it is air in the overlying lung.

These are the films taken at the time of the second admission; they show a large amount of fluid in the pleural cavity and disease in the right lower lobe. The mass and the shadow, which is either air or fat, are still present.

This view, with the patient on his side, was taken after a tap to determine whether there were pleural metastases. There are irregularities along the pleura, but they are most likely masses of fibrin rather than metastases, because fibrin is usually present with bloody fluid. One cannot, however, positively rule out metastases.

Dr. Brues: I am going to let my diagnosis rest on the history rather than on the location and to assume that the tumor arose near the bronchi rather than posterior to the pleura. I shall say that it was a teratoid tumor.

Dr. Richard H. Sweet: Might I say as a representative of the service that saw the man before he was operated on that we did not believe, at least I did not believe that he had a benign tumor. In fact I have never seen a benign mediastinal tumor produce bloody effusion. My personal diagnosis was, and I suspect some of the others who saw the patient were of the same opinion, a malignant tumor, probably teratoma. Dr. Brown operated on this patient. What does he say?

Dr. Robert K. Brown: We did a thoracoscopy and did not see much except a large empty space with implants of fibrin on the chest wall. Biopsies were taken of these and they were not malignant. Since we still thought that the tumor was malignant, the patient was explored.

The preoperative diagnosis was malignant neurogenic tumor or neurofibrosarcoma, because we thought that it arose in the posterior mediastinum.

At operation there was a large cystic mass in the upper part of the right thorax. This contained a hole, and the rupture was probably the cause of the bloody pleural fluid. A biopsy specimen was taken from the wall of the cystic mass at the edge of the rupture, and on cutting, it was evident that there was lung tissue adherent to the wall of the mass. I thought this was collapsed lung plastered over the cyst. The patient died following operation.

Dr. Benjamin Castleman: Would anyone want to venture a diagnosis at this point?

Dr. Ralph Adams: I have no idea what was wrong with this man. I think that the lesion arose in his lung because of two factors that almost have to place it in the lung. First, there was frequently recurring hemoptysis. There was a rule here a few years ago that daily hemoptysis meant carcinoma. After three years we found an exception in a case of bronchiectasis. That was the first exception, and I have since encountered one other. In the second place, this man had a wheeze, indicative of developing bronchial obstruction. My personal diagnosis, if I were about to operate, would be slowly growing sarcoma of the lung. I believe that sarcoma in the lung has occurred in this hospital only once.

Dr. Sweet: That is correct.

Dr. Robbins: How do you explain the erosion of the pedicle of the fourth thoracic vertebra if it is a primary lung tumor?

Dr. Adams: I could not explain it as a primary lung tumor unless it were sarcoma of the lung. If it were a sarcoma arising in the mediastinum and invading the lung the explanation would be easy.

Dr. George W. Holmes: Is there anything to show why there was such a delay between the first roentgenologic examination and operation.

Dr. Castleman: The patient refused operation.

CLINICAL DIAGNOSIS

Superior mediastinal tumor, with rupture into the pleural cavity.

DR. BRUES'S DIAGNOSIS

Teratoid tumor of mediastinum, with rupture into the pleural cavity.

ANATOMICAL DIAGNOSIS

Neurofibroma of lung, with cystic degeneration and rupture into the pleural cavity.

PATHOLOGICAL DISCUSSION

Dr. Castleman: The material that Dr. Brown removed from the cyst or tumor was composed of spindle-shaped cells, some in whorls, which strongly suggested neurogenic benign tumor. In favor of this was the presence of huge numbers of so-called "foam cells," that is, large lipoidladen mononuclear cells. That is probably the reason why Dr. Robbins thought he saw fat in the tumor. Certainly a large part of the tumor was composed of cells filled with fat. Lipoid degeneration of a neurofibroma is not at all uncommon. We were fairly certain that the tumor was benign.

The autopsy specimen shows that this tumor was within the lung. It had broken down so much that it had become cystic. This cystic mass, which was about 7 or 8 cm. in diameter, communicated with the apical branch of the right upper lobe bronchus, and this certainly

accounted for the long-standing hemoptysis. I believe that the tumor probably arose close to the bronchus, or perhaps in it, and degenerated slowly as it gradually increased in size. There was lung tissue surrounding the cyst on all sides except over the area where it had ruptured.

We have had 2 other cases of neurofibroma of the lung. One was in a man of thirty who had all the signs and symptoms of a bronchial adenoma, that is, bronchial obstruction with hemoptysis. Bronchoscopic biopsy showed it to be a neurofibroma, and Dr. Benedict removed the tumor via the bronchoscope in three operations.

Dr. Edward B. Benedict: The patient was completely relieved by bronchoscopy. I have not seen him for three years. He had no apparent lung damage.

Dr. Castleman: The other case was one in which Dr. Churchill performed a lobectomy for a well-circumscribed tumor that pressed on a bronchus but had not acutally invaded its mucosa.

BOOK REVIEW

New and Nonofficial remedies. Issued under the direction and supervision of The Council on Pharmacy and Chemistry and American Medical Association. J. B. Lippincott Company Philadelphia 1951.

This volume is too well known to most physicians to require extensive comment. It is pleasant to note that the authors are apparently on the alert for means of improving the book as each edition seems to show considerable improvement over the previous one. In the preface the authors invite criticism with a view to further improvements of the book. The book is really divided into four parts, the first part giving the names of the members of The Council on Pharmacy and Chemistry with their consultants and outlining the purposes of The Council on Pharmacy and Chemistry and giving the requirements for admission of articles to this volume. Other information such as general provisions and labeling requirements is also found here.

The next section is called section "A" and entitled Accepted Products. Here the products are listed according to their place in 23 classes

of drugs or therapeutic agents. As an example of the type of classification used the drugs are listed under such classifications as analgesics, anesthetics, antispasmodics, autonomic drugs, contraceptives, diuretics, etc. Here are the essential therapeutic information about the drugs is found and the preparations made by various manufacturers are listed.

In section "B" the tests and standards for non-official products are given. I think this was an improvement to place this information in a separate section since it is readily available here and does not get in the way when one wishes to read up on a drug for therapeutic purposes only.

Section "C" contains a comprehensive bibliography with reference to the products listed. There is also an index to distributors of the preparations listed as well as a very good general index.

This is valuable up to date reference material. I think every physician who has this volume available will find himself referring to it frequently.

THE *Secretary's* MESSAGE

NATIONAL ADVISORY COMMITTEE TO SELECTIVE SERVICE SYSTEM

Bulletin Volume II, No. 7

Release from Service

Navy Policy regarding physicians and dentists (former registrants and reservists):

Priority I 24 months

Priority II 12-24 months

Priority III 24 months

Priority IV

(12 months during World War II).....12-17 months

(Less than 12 months during World War II).....12-24 months

Army policy:

Any physician or dentist who served 12 months during World War II becomes eligible for release after 17 months of current service, except those called in Organized Reserve Units, who will serve the full 24 months.

Air Force policy:

Any physician, dentist or veterinarian may request release after 21 months of service. If he was in Priority I or II the 21 months must be during the present term of service.

Induction Group

Requests for delay in active duty orders, asked for some of those physicians who accepted commissions after receiving orders for induction and before being inducted, have been determined "entirely out of order" except under very special extenuating circumstances. Health Resources Advisory Committee is calling all records of such cases to Washington for review.

Physician Draft

Planned induction under Selective Service of 333 Priority I medical officers scheduled during the month of August has been delayed temporarily at request of Department of Defense. This delay is based entirely upon an unanticipated and sustained increase in number of doctors applying for Reserve Commissions in the Armed Forces. Whether doctors whose induction was delayed during August will be called during September is dependent upon volunteer rate during next few weeks. No reduction anticipated for call of 152 Priority I doctors scheduled to be inducted in September.

Physician Inductions

Many special registrants ordered by their local boards to report for induction on the July call for 717 doctors were found to have been previously commissioned. Since the July call, the Armed Forces have commissioned 429 doctors. Of this number, 333 received Army commissions, 186 Air Force, 3 Navy, and 7 were commissioned by the United States Public Health Service. Incomplete state reports disclosed that 10 doctors were declared physically unfit; 80 were reclassified, postponed, or cancelled; 2 were inducted; an indefinite number are still pending for one reason or another; and another very small number are believed to be delinquent and will be reported as such by their local boards. Of the two inducted, it has recently been reported in the public press that one of them agreed to accept a commission after completion of 3 days' service as an enlisted man.

Editorial

ARIZONA MEDICINE

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

CAREFUL, DOCTOR!

In recent years the number of organizations who are interested in the medical patient's welfare has increased tremendously. Besides the insurance companies who have long been with us we now have such organizations as American Cancer Society, Foundation for Infantile Paralysis, American Heart Association, and numerous other welfare agencies from the national level

on down to the local levels. There are various disease registries such as the Tumor registry and the cancer registries in various states.

Any physician may receive requests from any or all of these agencies for information about his patients and these requests may become so numerous and so routine that their validity may be taken as a matter of course. The physician is then on dangerous ground as he is dealing in privileged communications under the law and should he neglect to obtain a release from the patient before he supplies the information requested he is leaving himself open to legal action.

Many times the person or organization requesting the information, because their interest is valid and humanitarian, apparently feel that they are exempt from this rule. A single illustration will demonstrate this. During the last war I had a patient who was dying of cancer. She had a son on duty overseas in the armed forces. The Red Cross was trying to obtain a leave of absence for the boy to visit his mother. I knew nothing of this until I received a call from the Red Cross asking for information about the patient. The young lady who called was quite surprised when I insisted on a release from the patient and replied to my insistence by informing me somewhat haughtily "Why, this is the Red Cross." I patiently explained to her that no matter how high her motive, how worthy the cause, or how poignant the situation, that nevertheless the fact remained that I was dealing in a privileged communication and would need the patient's permission for its release.

There are very few occasions when you can legally reveal information about your patient without his consent. Even on the witness stand in court you are not required to do so unless ordered to by the judge. Ordinarily you may answer safely in court as the failure of your patient's counsel to object to a question implies his consent for you to answer it. If there is any doubt however in your mind, indicate that you consider this something you cannot answer without consent of the patient and ask the judge for a directive. If he orders you to answer you are legally absolved of the consequence.

The growing desire of the medical profession for better public relations and particularly as it concerns better cooperation with the newspapers in news of prominent individuals can be a trap and a snare. The press has long contended that doctors are too close-mouthed and "standoffish" and will not supply the news which "the public deserves". The physician

caring for a prominent patient, anxious to offset this feeling of the press may easily be led to divulge something as news to which the patient may object.

So! Careful Doctor! Don't let your guard down. The law hasn't changed. Check before you chat—Think before you talk, and above all—get that release from your patient.

TOPICS OF *Current Medical* INTEREST

DX, RX, AND DRS.

By GUILLERMO OSLER, M.D.

Mrs. Royal Rudolph is the president of the WOMAN'S AUXILIARY to the Arizona Medical Ass'n. If she were asked to urge the women members to read ARIZONA MEDICINE, is COULD start a whole sequence of events,—the women members would read the journal; they would note the rarity of papers by physicians from Arizona; their husbands would then hear about it at home; more surveys and pieces of research would be started; and ARIZONA MEDICINE would eventually get more papers written by home talent. . . . Thank you, Mrs. Rudolph.

The pattern of susceptibility which allows so many young American men to have CORONARY ARTERY DISEASE has been worked out in the M.G.H. in Boston, under the guidance of Paul White and summarized by Gertler. . . . Individuals who are likely to have myocardial infarction can probably be identified well in advance of such illness. . . . The formula contains data on body build, physiology, personal history, heredity, and sociologic status.

Literature in favor of TUBERCULOSIS CASE-FINDING programs in the United States has made much of the fact that the disease is sometimes not officially known until death. . . . The publicists never had such good ammunition as the Arizona figures. The public health authorities first hear about at least 55 per cent of the tuberculosis cases when the death certificates are filed. . . . This column has pleaded for better reporting of the disease, and does so again. If a physician knows of a case, and if the patient is infectious and in uncontrolled contact with others, and if no report is made, it is akin to homicide with an accessory before the fact.

The Minnesota Medical Journal reports that the Hennepin County TB Ass'n. has started a campaign to have all Minneapolis hospitals X-RAY ALL NEWLY ADMITTED PATIENTS. . . . Very laudable. The paradox would seem to be that

J. Arthur Myers has almost convinced people that Minnesota doesn't HAVE any tuberculosis. . . . Maybe the survey is aimed at Loeffler's syndrome or *Paragonamus Westermanii*.

SWELL SMELL QUELLS have been announced by two responsible companies. 'Odorant' is a 3½ watt lamp which can be placed in a wall fixture, and which is said by Westinghouse Electric Corporation to change the odor molecules of cooking, smoking, dampness, perspiration, etc., by the output of ozone. . . . 'Aero-Klenz Gel' is sold by the American Hospital Supply Corporation. It is said to deodorize putrid lesions for eight hours or more, and to be non-irritating.

More data are now available (in 'Anaesthesiology') on the narcotic DROMORAN HYDROBROMIDE. The drug was mentioned here a year ago. . . . It was used in 1,500 patients as a pre-operative medication, usually with atropine or scopolamine. The effect was unsatisfactory in 6.5 per cent, but almost all of these were due to lack of experience in dosage. . . . Nausea was very rare (1 case); pain and anxiety were absent; euphoria, hallucinations, and disorientation were not noted; and the patient could respond tho drowsy. . . . Sounds good so far.

The names of the ASSOCIATES IN GREAT MEDICAL DISCOVERIES often slide into limbo, except perhaps to people closely concerned. . . . Who, for instance, are Chain and Heatley? They were colleagues of Florey at Oxford who helped purify and first use penicillin. . . . Who were/are Slocumb and Polley? More familiar, but not as well known as their chief Hench, when they all demonstrated the use of cortisone and ACTH. . . . Then there is the man who refused to stay unrecognized, and sued Dr. Waksman, whom he helped discover streptomycin. So we've forgotten his name entirely!

The Sharp & Dohme publication reports that

*Effective against many bacterial and
rickettsial infections, as well as certain protozoal
and large viral diseases.*

AUREOMYCIN

Hydrochloride Crystalline



The Gastroenterologist

recognizes the remarkable inhibiting effect of aureomycin on a great number of organisms, especially those commonly found in the gastrointestinal tract. It is of great value in the preparation of patients for surgery of the bowel or biliary tract, as well as in the medical management of infections in these areas. Aureomycin is also highly effective in intestinal amebiasis. Aureomycin is peculiarly adapted to the treatment of many biliary and hepatic infections, because of the high concentrations it attains in the bile and because of its protection of the hepatic parenchyma from bacterial necrosis. Aureomycin is indispensable in gastroenterology.

Packages

Capsules: Bottles of 25 and 100, 50 mg. each capsule. Bottles of 16 and 100, 250 mg. each capsule.
Ophthalmic: Vials of 25 mg. with dropper; solution prepared by adding 5 cc. distilled water.

LEDERLE LABORATORIES DIVISION

AMERICAN Cyanamid COMPANY

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NYLON fiber (DePont) is not a cause of dermatitis. Any dermatitis which results from wearing a nylon garment is due to the finishing or dyeing of the product.

The Danes report a new antibiotic 'LEOCIL-LIN', which has a marked predilection for lung tissue. It is a form of penicillin (to be precise, benzyl-penicillin-beta-diethylamino-ethylester hydriodide). . . . Ten times as much of the drug may be found in the lungs as of penicillin, tho the other organs have similar amounts. . . . It is excreted in the sputum, and naturally could be of great value in lung and bronchial infections.

TERRAMYCIN is being found effective in a variety of conditions. It is said to be rapidly effective in whooping cough. It is said to be very helpful in ulcerative colitis (tho one remembers the psychic element in the disease, and the obstacles which a chronic case would present). Cholera is susceptible to the drug. Finally (and most importantly to brook trout) terramycin is the only agent which cures 'ulcer-disease' in brook trout.

Chest specialists are hearing from their patients about a new anti-TB drug from Sweden. Now they may hear it from here. . . . 'PROTAP-TIN' was discovered by Davide and Theorell, and reported in Rome in June 1951. It has the same build-up as neomycin, viomycin, et al. Very good in cultures and animals, but we'll have to see later. . . . Could be used for the high incidence of streptomycin resistance in admissions to some V.A. hospitals (50%).

A question was asked in this column two years ago about the possible **ADDITION OF AN EME-TIC TO SLEEPING CAPSULES**. . . . Such capsules, containing ipecac with the barbiturate, have been on sale for two years. . . . They have been disapproved, however, since ipecac itself is toxic, and since the absorption and action would be slow enough so that too much sedative would also be absorbed. . . . J.A.M.A. Queries and Minor Notes now mentions that zinc sulfate is a better drug than ipecac. It works faster in producing emesis, and is non-absorbable. . . . Perhaps the objections to this idea will come sooner than 2 years.

What a Long Tail Our Cat Has.—Ideas for water saving, water production, water importation, etc., continue to appear. So far they are not yet enough. . . . 'Tax Talk', a Los Angeles publication, totals the cost of Colorado River water, Flood Control, and Sanitation Districts. It

is huge. . . . What interests Californians also interests Arizonans, and the plea of Tax Talk is not for more water sources but **DOUBLE USAGE** of what they have. How can used clean water from households be returned to the ground instead of being channelled to the sea?

A member of Alcoholics Anonymous has certain select qualifications,—he must have been an alcoholic, he must be cooperative, and he must be the type who responds to the religious appeal. . . . Consider how specialized a person must be who attends the SECOND INTERNATIONAL Conference of PHYSICIAN MEMBERS of ALCOHOLICS ANONYMOUS, at CLAYTON, New York, in August. . . . However there are 200,000 physicians in the United States, and more than a few have been known to take a drink.

BERYLLIOSIS has been a recent sensation in the 'new disease' field. The greater use of beryllium and the bizarre aspects of the lesions makes the conditions notable in medicine. . . . Now we find a medical use for beryllium, as described in a Machlett bulletin, the 'Cathode Press',—A new x-ray tube, containing a beryllium window, is made by them. It produces low-voltage radiation, and many superficial lesions are amenable to such x-rays, since they may be confined to a small surface area.

A new CANINE ANTIRABIES VACCINE, is 'strictly for the birds', but it eventually 'goes to the dogs'. . . . This paradoxical pun arises from the fact that the vaccine is 'avianized' or produced by growth in chick embryos. Contrary to the usual vaccine, it contains a live attenuated virus, and its effects also seem to last longer than the usual one year. . . . It is designed for prophylactic use in dogs, the species which is the major vector. . . . The U. S. Bureau of Animal Industry has released it for a controlled usage, and California State Health Department has distributed almost 3,000 doses.

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S.1186 AND H.R. 3298

Statement of Dr. Walter B. Martin on Behalf of the American Medical Association Regarding S.1186 and H.R. 3298, 82nd Congress Before a Subcommittee of the Senate Committee on Labor and Public Welfare.

Mr. Chairman and Members of the Committee:

My name is Walter B. Martin. I am engaged in the active practice of medicine in the state of Virginia and am a member of the Board of Trustees of the American Medical Association. I am appearing here today on behalf of that Association regarding S.1186 and H.R.3298.

Before proceeding, I would like to express the appreciation of the American Medical Association for the privilege of presenting a statement on these bills.

The substitute version of S.1186 as introduced on July 5, 1951 is designed to accomplish several purposes. The bill would amend the Federal Food, Drug and Cosmetic Act by expressly writing into law, provisions dealing with the labeling and dispensing of drugs which may be sold on prescription, and drugs which may be sold "over the counter." The Administrator of the Federal Security Agency would be given the authority to determine which drugs are unsafe and ineffective for use without professional diagnosis or supervision and thus to classify drugs into two groups on an arbitrary basis. The bill also provides that a qualified prescriber of drugs may telephone a prescription to a pharmacist, provided the pharmacist promptly reduces the prescription to writing and files it. If the original prescription was for a drug determined to be safe and effective for lay use without medical supervision, the bill authorizes the druggist to refill the prescription without confirmation from the physician. However, as to drugs which are habit forming or which are safe and effective only after medical diagnosis and supervision, the bill prohibits the refilling of prescriptions without expressed written or oral authorization by the prescribing physician.

On June 14, 1951, the Board of Trustees of the American Medical Association expressed their approval of the majority of the objectives sought by this legislation. This position was reaffirmed by the Executive Committee of the Board on August 4, 1951. The Association sup-

ports the provisions of the bill authorizing the filling and refilling of oral or telephone prescriptions. We also approve the restrictions pertaining to prescriptions for dangerous drugs. However, the Association is unalterably opposed to the provisions of the bill which give the Administrator of the Federal Security Agency dictatorial power to decide which drugs must be sold only on prescription and which must be labeled for "over the counter" sale. The delegation of such authority to the Federal government is believed to be extremely dangerous and wholly unwarranted.

It has been estimated that if this bill is enacted, it will be necessary for the Food and Drug Administration to promulgate regulations classifying over 30,000 drugs, and thus to specify the manner in which they may be dispensed. The necessity for continuous reference to such a list and to current official regulations in this regard would place a tremendous burden on the average druggist. The immensity of the task would inevitably result in technical violations, of no public health significance and would probably require the addition of numerous enforcement officials to police the procedure.

A more basic objection to the provision in question is that it vests in the Federal Security Agency, control of the drug industry and delegates to that agency the power to determine the therapeutic value of drugs—a decision which is a traditional and time tested function of the medical profession. In this respect federally placed control of the drug industry, especially as to the effectiveness of drugs will result in unnecessary and undesirable control of the practice of pharmacy and the practice of medicine.

There is also pending before your Committee another bill, H.R.3298, which was passed by the House of Representatives on August 1, 1951. This bill was amended on the House Floor so as to strike out the provisions which would give the Federal Security Administrator power to classify prescription and non-prescription drugs, to which our objections are directed.

The American Medical Association favors the enactment of H.R.3298 with one minor amendment. It is suggested that a period be placed after the word "sentence" on page 3, line nineteen, clause (b) (4) and that the following words beginning on line 19 and continuing through line 22 be eliminated: "or any other



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statement which represents or implies that the dispensing of the drug without the prescription of a licensed practitioner is prohibited." It is believed that this wording is ambiguous and unnecessary. The prohibition against the improper use of the caution legend included in the same sentence should provide a sufficient safeguard.

Again let me thank you for affording us the opportunity to present these comments.
September 13, 1951

REGIONAL MEDICAL MEETING

The Coconino County Medical Society joined the Medical Societies of the five Northern Counties Wednesday, October 3rd, in a Regional Meeting at the Bright Angel Lodge at Grand Canyon. The meeting, organized by Dr. Leo Schnur, President of the Coconino County Medical Society, had as its general theme the topic, "Psychotherapy in General Medicine."

Registration was held in the morning, followed by luncheon. Dr. Harold C. Bryant, Superintendent, National Park Service, Grand Canyon, delivered a welcoming address to the visiting doctors and wives.

Guest speaker was Dr. Hale F. Shirley, Associate Professor of Pediatrics and Psychiatry at Stanford University and Director of the University's Child Guidance Clinic in San Francisco. Dr. Shirley stressed the importance of the non-psychiatric physician's role in dealing with the emotional aspect of his patient's illness. Dr. Clarence Salsbury, of the Arizona State Department of Public Health, acted as moderator and led the group in general discussion following Dr. Shirley's remarks.

Dr. Henry C. Schumacher, San Francisco, Medical Director of Region 10 of the U. S. Public Health Service, also spoke to the group.

Notable among the physicians present were Dr. Dermont W. Melick, President of the Maricopa County Medical Society; Dr. Charles W. Sechrist, Flagstaff; Dr. Herbert R. Rice, Flagstaff; and many leading doctors from most of the counties in the state. Mr. William B. Macomber, Supervisor of Mental Health, State Department of Health, Phoenix, and Miss Courtney Rettger, Tucson School System psychiatric social worker, contributed remarks to the general discussion.

The doctors' wives were entertained at bridge during the afternoon at the El Tovar Hotel.

The medical group enjoyed a social evening following dinner at El Tovar.

SCHOLARSHIP IN PSYCHIATRIC NURSING

Word has been received from the ARIZONA FEDERATION OF WOMEN'S CLUBS that a \$500.00 Scholarship in Psychiatric Nursing is now available to a graduate nurse who will give the benefit of this training in Arizona.

This program of the Arizona Club is part of a National Program sponsored by the GENERAL FEDERATION OF WOMEN'S CLUBS. Facilities of Louisville's Norton Memorial Infirmary Psychiatric Clinic, in Louisville, Kentucky, are being made available to nurses from all sections of the nation for postgraduate psychiatric nursing education. The Norton Psychiatric Clinic is recognized by the Division of Nursing Education of Columbia University, New York City. Under provisions of the National Mental Health Act, there are provided clinical instructors for teaching psychiatric nursing, and resident fellowships for doctors completing their formal psychiatric education.

Nurses will be accepted for instruction at intervals of two months. The course, centering in the Norton Psychiatric Clinic, is amplified by coordinated training at Louisville General Hospital, the Mental Hygiene Clinic, and the Child Study School.

For additional information and application forms, contact:

Mrs. Hazel D. Smith, Scholarship Chairman
Arizona Federation of Women's Clubs
501 East 16th Street.
Tucson, Arizona

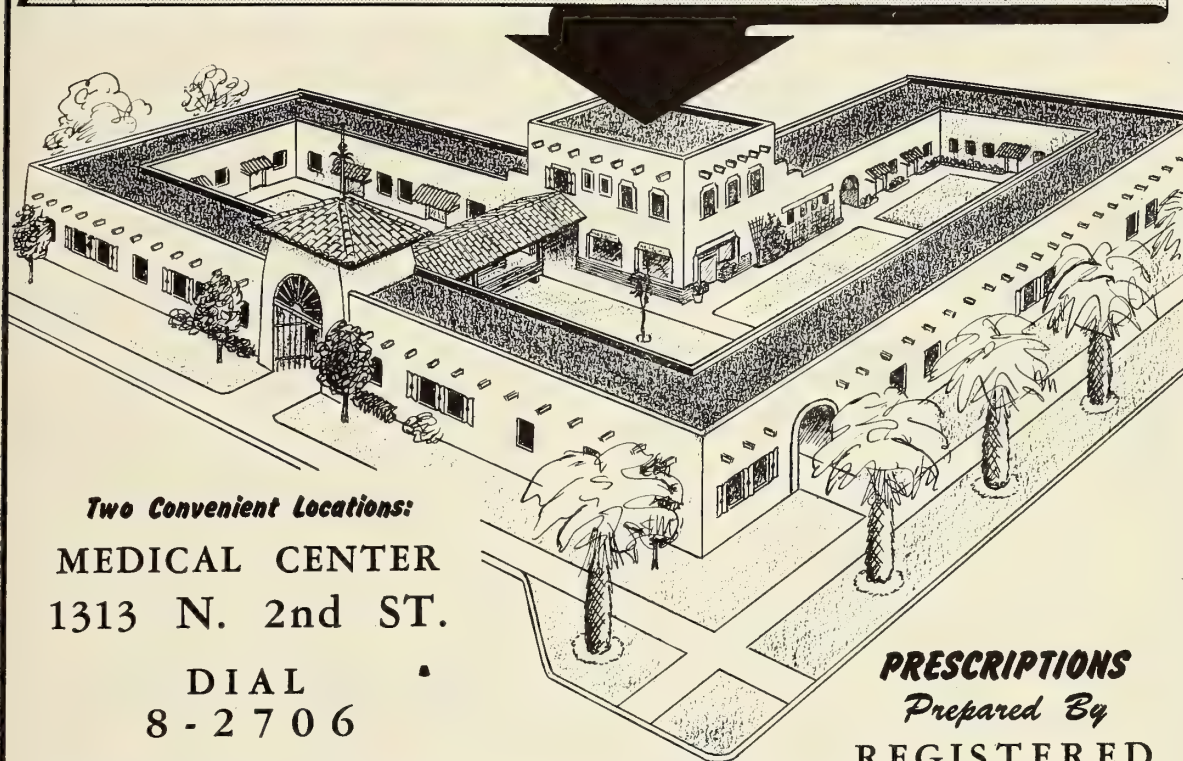
PERSONAL NOTES

Dr. Henry A. Siegal, 15 East Monroe Street, Phoenix, Arizona, has recently returned from Chicago where the degree of Certified Fellow of the International College of Surgeons was conferred upon him.

Dr. and Mrs. Kenneth C. Baker have returned from El Paso where they attended the meeting of the Southwestern Dermatological Society which convenes in conjunction with the Southwestern Medical Association. The meeting was held at the Hotel Cortez Saturday and Sunday, October 20 and 21.

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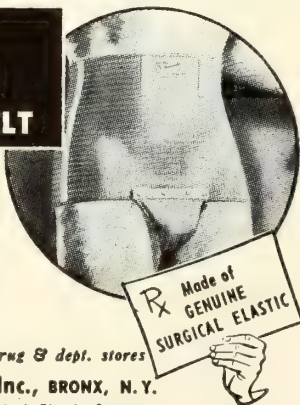
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AMERICAN CANCER SOCIETY

A statement of the aims and objects of The American Cancer Society, Arizona, Division.

The American Cancer Society, through its representative organization, the Arizona Division, solicits the cooperation and support of all physicians in the State of Arizona. As is logical, the primary aim of the American Cancer Society is to discover, through research, the cause of cancer. It is proper that the greatest effort of The American Cancer Society should be in the direction of research. Until the day when cancer can be eliminated the American Cancer Society stresses, as its second great aim, the early recognition of cancer so that it may be adequately treated. Its educational program, therefore, embraces all aspects of the cancer problem from cancer education at the physician and medical school levels through cancer education of the general populace down through the school child. With that in mind every medium is used and the general population has become aware of the so-called "Seven Danger Signals". The importance of these two major programs becomes apparent as cancer rises in the list of causes of deaths to a higher and higher position, not only because of the elimination of infectious diseases and other previously more significant causes, but also because more people now are entering the older age groups where cancer is more prevalent.

The third phase of the cancer program is the service program. This includes the provision of financial aid and assistance to those suspected of having cancer who require diagnostic studies and hospitalization and in some instances assistance in proven cases of the disease. Dressings are provided when necessary and the program includes the maintenance of such detection centers as are operated in our area. Of necessity the service program is limited in its scope for the funds available to the American Cancer Society are in no way comparable to those raised by other similar health organizations. The service program in its application is offered to those individuals who are unable to pay for similar services in the usual manner and who are not eligible for care in county hospitals, governmental institutions or through assistance from families.

It must be apparent from the above that the first and second aims of the American Cancer

Society should be given preference. The service program must be curtailed because of lack of funds. In actual operation requests for service help should indicate the name of the attending physician or recommendation of the cancer clinic or detection center. Such requests for assistance should be directed to The American Cancer Society, Arizona Division, at 25 East Van Buren Street, Phoenix, Arizona, or to the local representative of that society in each county. In general social service information and welfare records give information to confirm that help is being given to needy individuals, and such a survey is necessary to assure the proper distribution of help. Service funds can be applied in amounts usually limited to \$75 or \$100 per case, with a few exceptions, and these funds are paid to hospitals or diagnostic organizations upon billing. Physicians have universally offered their services to such indigent patients without charge.

It is the hope of the Professional Board of the Arizona Medical Association that each doctor's office throughout the state will become the primary initial detection center. Cases suspected of having cancer and requiring help from the American Cancer Society it is hoped will be promptly cared for. Thus the American Cancer Society will have the opportunity to contribute to the early recognition and proper treatment of all malignancies.

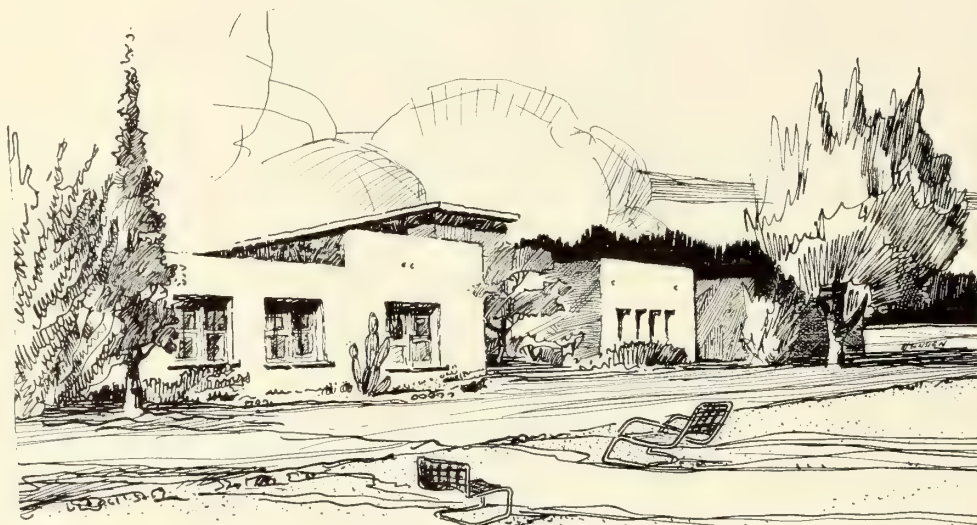
ARIZONA HEART ASSOCIATION

The annual meeting of the Arizona Heart Association was held in Phoenix, Arizona, Saturday, September 29, 1951, at Hotel Westward Ho. Following opening remarks by Benson Bloom, M.D., Tucson, Program Chairman, John C. Jones, M.D., of Los Angeles, Associate Professor of Surgery, University of Southern California, discussed "Congenital Heart Surgery." His address was followed by Louis N. Katz, M.D., of Chicago, Illinois, President of the American Heart Association, who discussed "Recent Trends in Clinical Electro Cardiography," and "Recent Developments in Atherosclerosis." John C. Jones, M.D., presented further discussion on "Mitral Valve Surgery."

Dr. Clarence L. Robbins of Tucson succeeds Dr. Kent H. Thayer of Phoenix as President of the Heart Association and will lead this Association's efforts to raise \$30,000 in a campaign to be

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inaugurated in February, 1952, for the fight against heart disease. Dr. Robert S. Flinn of Phoenix was named President-Elect to succeed Dr. Robbins next October. Other officers for the coming year are Dr. Ben P. Frissell of Phoenix, Vice President; Robert H. Whitacre of Phoenix, Vice President of the First National Bank of Phoenix, Treasurer; Miss Elizabeth Rockwell, Secretary; and George F. Stoeberl, Executive Director.

FROM SECRETARY LULL'S LETTER

Tells What Makes A.M.A. Tick. President John W. Cline gave an excellent and most interesting address before the annual session this week of the Medical Society of the State of Pennsylvania at Pittsburgh. His title was "You Are the A.M.A."

He recounted the part which Pennsylvania physicians have played in the growth of the A.M.A. and then pointed out some of the responsibilities which doctors have toward their national association.

"The responsibilities," he said, "are yours because YOU are the A.M.A. As an individual, as a county medical society member, as a state society member . . . YOU are the A.M.A. You elect its officers, promote and implement its program, and finance its activities through your annual dues. You share in its accomplishments and, by the same token, you must share the criticisms levied against it.

"In an organization as large as ours, it is regrettable that so few do the work for so many. How many times have you heard your minister preach on church attendance? Invariably, he says that, to his sorrow, the members of his flock he really wants to reach are the ones who aren't in the church.

"In the same way, I can say that the majority of the physicians here today are the workers . . . the men who constantly give their support and assistance to the A.M.A. and their county and state societies. For that reason, this meeting can be more accurately classified as a sales conference. You are the A.M.A., and it's up to you to carry the information you receive today back to the hundreds of physicians in Pennsylvania who don't attend state meetings."

Dr. Cline listed several specific criticisms leveled at the A.M.A. and the medical profession, and told what should be done to correct

the trouble. He concluded by saying that "every physician should work closely with his national organization to correct the misunderstandings that prompt criticism of our profession."

"Unfortunately," he added, "the basis of most misunderstanding either begins to germinate or could be clarified during the initial visit of the patient to his doctor. You are the A.M.A. to your patients and whatever they think of our association . . . and our profession . . . will depend on your personal responsibility as a good will ambassador."

Dr. W. W. Bauer, director of the A.M.A. Bureau of Health Education, spoke at the same session. The title of his talk was: "What Do You Get For Your \$25?" He did a fine job of explaining the many services which are available to physicians through their national association.

At about the same time, Dr. Edward J. McCormick of Toledo, a member of the Board of Trustees, gave a talk very similar to Dr. Cline's before the annual session of the Colorado State Medical Society in Denver. His speech was also entitled "You Are the A.M.A."

Dr. McCormick said that he was willing to wager that "if someone stopped you on the street and asked, 'Say, Doctor, just what is the American Medical Association?', you'd come up with a long explanation about our Chicago headquarters and our hundreds of activities."

"To my way of thinking," he said, "you'd be wrong. The A.M.A. isn't a big stone building in Chicago; it isn't a bunch of councils and committees and bureaus all lumped together. Doctor, the A.M.A. is YOU. You are the A.M.A."

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Front Row: Seated, Shirley Koluch, Phoenix, Arizona; Joan Nasser, Miami, Arizona; Frances Lopez, Morencí, Arizona. Back Row: Standing, Mary Gustafson, Tucson, Arizona; Jackie Johnson, Phoenix, Arizona. Mary Gustafson is in training at Good Samaritan Hospital. The other girls are at St. Joseph Hospital. These are all the student nurses in training in Phoenix. There is one in Tucson who is not shown here.

STATE NURSES' LOAN

To the doctor's wives in the state of Arizona the Nurses' Loan Committee of the Auxiliary to the Arizona Medical Association makes a direct appeal for help and co-operation. The Nurses' Loan program is beginning its second active year, but it needs the assistance of all doctors' wives to publicize the program. Will you, after you read this article, go to the Clubs and various organizations in your community and explain the program? Also, will you go to your high school principals, high school nurses, and vocational directors and tell them of the availability of the loan for worthy girls who wish to become nurses? We have sent letters for the past two years to all high school principals in the state telling of our loan fund, but we know that the personal approach brings better

results.

Here is a list of our requirements:—

1. The applicant must have a B average
2. The applicant must pass a strict physical examination
3. The applicant must *need* the loan
4. The applicant must be of good moral character and must furnish three character references, one of which must be from a member of the high school teaching staff
5. The applicant must have a parent or guardian co-sign with her to agree to repay the loan. The maximum loan granted is \$300, interest free. The applicant must agree to repay the loan at the rate of not less than \$12.50 per month. She must start repayments within six months after she receives her state license to work.

If she does not finish training, the applicant must agree to start repayment of the loan within thirty days after leaving the School of Nursing

6. The applicant must be accepted by one of the four accredited Schools of Nursing in Arizona. These are:—St. Joseph's Hospital, Good Samaritan Hospital, Memorial Hospital (all in Phoenix) and St. Mary's Hospital in Tucson, Arizona.

Last year the Nurses' Loan Committee gave financial help to four girls. This was the first year of the program. We gave loans to two girls in training at Tucson, and to one girl at Good Samaritan Hospital in Phoenix. This girl was second highest in her class. We also gave a loan to a girl at St. Joseph's Hospital. This fall the Committee voted to give loans to three girls, one from Morenci, one from Miami, and one from Phoenix. They entered St. Joseph's School of Nursing on September 19, 1951.

Pima County Auxiliary will have a large tea in October and will invite junior and senior girls who are interested in becoming nurses to attend. Maricopa County probably will have a similar function. Please inform your Community of the program so that the Auxiliary can contact and help more worthy girls to become nurses.

Respectfully,

Josephine B. Craig

(Mrs. Carlos C. Craig)

Chairman State Nurses' Loan Committee

GETTING THE MOST FROM YOUR BULLETIN

The Bulletin, well known as the official publication of the Auxiliary, gives to the membership information and suggestions that will be of interest to them and help them in their work. In order to keep informed and up to date, one must acquire the habit of reading the publication.

From the pages of the August issue let me acquaint you with some of the worthy projects accomplished in other states.

In California, Civilian Defense is a vital new project which has been added to their agenda. Auxiliary members have been working as individuals in various community capacities, but as auxiliaries have been requested to make master files of all nurses, registered and practical, with

pertinent information as to training and availability. One county sent questionnaire cards to all members to ascertain abilities, training and interests in connection with Civilian Defense.

The inadequate care of the mentally ill is by far the greatest health problem in the State of Florida. A State Mental Health Society was organized and a member from the Auxiliary executive board was appointed legislative chairman for this committee. Information concerning present conditions with proposed legislation for the correction of same were sent to every organization throughout the state. The legislative chairman of the Auxiliary has worked with the Mental Health Society in obtaining public support of proposed legislation. There is a definite awareness among those with political ambitions of the existence of a medical Auxiliary in the State of Florida.

Nurse recruitment has been a major project for the State of Kansas. Most of the auxiliaries included a program on nursing. In 15 counties, 22 scholarships have been developed, 12 counties sponsored programs in high schools to interest girls in nursing, and 10 organizations presented films on nursing to all the high schools in their counties.

Louisiana's nurse recruitment program has expanded due to the outstanding work of the medical auxiliary. The schools of nursing showed the highest percentage increase in admissions of new students of any state in the country last year, with a 53% increase over 1949 and a total of 741 first year students. Programs varied throughout the state. One auxiliary had a window display in a leading department store, while another depicted the story of the shortage of nurses in a Junior Chamber of Commerce 'Democracy versus Communism' parade. Literature on nursing and against compulsory health insurance was distributed to thousands of on-lookers.

Kentucky became aware that most of the college and university editors in this country were receiving from various sources much socialistic propaganda to be used either in the student publications or as material for programs on the campus. In order to offset this propaganda the auxiliary sponsored a college Editors' Contest on Americanism in senior colleges in Kentucky. Every editorial staff of every senior college was visited personally and the purpose

of the contest was explained to them. They felt that in this contest "seeds of inspiration were sown in the minds of many college students who might otherwise have been indifferent."

"Health Days", of which Minnesota is so justly proud, continues to be their greatest contribution to public relations. These are sponsored jointly by the State Auxiliary, the State Medical Association and State Department of Health. Programs are made up of panel discussions, films concerning cancer, tuberculosis, accidents in the home and health programs concerning schools. Sanitation and legislation are discussed. Many county auxiliaries have "Guest Days" to which other organizations are invited to hear the best informed speakers on pertinent subjects

The activities in these states are but a few of possible lines of endeavor which may absorb the workings of the auxiliary. There are many others and we should surely never want for lines of achievement in our own auxiliary. Our organization is continually becoming more active and it is hoped that our future projects may be as well chosen and successful as the above-mentioned ones have been.

Irene R. Hewitt (Mrs. Roy)
State Bulletin Chairman

H.R.-910

FEDERAL AID TO NURSE EDUCATION

This bill provides federal aid to nursing education in four different categories:

1. Annual payments to schools for cost of instruction
2. Grants for construction and equipment of new schools or expansion of existing schools.
3. Scholarships.
4. Grants for a recruitment program.

Both proponents and opponents generally agreed that a shortage of nurses or nursing services exists but opinion varied as to degree, nursing schools are short of instructors and a proviso for a court appeal in the event funds are withheld by the government should be written into the bill.

Dr. Walter B. Martin, of Norfolk, Virginia, a member of the Board of Trustees of the American Medical Association, appeared before the interstate and foreign commerce committee to express opposition to many parts of H.R. 910.

The Association objected to intrusion of the federal government and its agents into fields of education whether it be general education, medical education or nursing education. This bill would give the Surgeon General of the Public Health Service, under the Federal Security Administrator almost unlimited administrative powers. Also with a system of subsidies established it will be difficult or impossible to terminate them once the schools have become dependent on a federal dole. Their sources of private support will wither, and their freedom will be lost because they will necessarily have to comply with every federal regulation or go out of existence. The American Medical Association feels that there is a present shortage of nursing service, although there is not an actual shortage of nurses. Of the 500,000 trained nurses in the United States there are approximately 300,000 who are following their profession, and the reserve of 200,000 nurses could be tapped in the event of a national emergency.

Dr. Martin proposed the following in lieu of H. R.-910:

1. One-time construction grants on matching basis, based on formula similar to that of the Hospital Construction Act. (Hill-Burton Bill).
2. A grant of federal funds to Committee on Careers in Nursing or some comparable private agency to help support a nurse recruitment program.
3. A temporary grant-in-aid program, not exceeding five years, of scholarships for advanced nursing education, administered by states.

A three point program of this type should provide for the construction of necessary additional nursing schools and the renovation of certain existing facilities; for a strong national promotion and information program to bring qualified young people into nursing, to improve the profession and encourage nurses to remain active in their profession; and for an increase in the number of qualified teachers in the nursing field. It is believed that these suggestions, if put into effect, would meet the current need and at the same time safeguard the freedom and independence of educational institutions far more satisfactorily and specifically than does H. R.-910.

Mrs. Louis Hirsch
State Legislation Chairman

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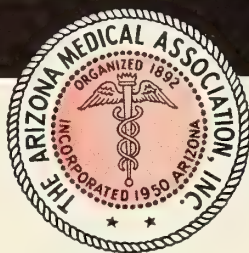
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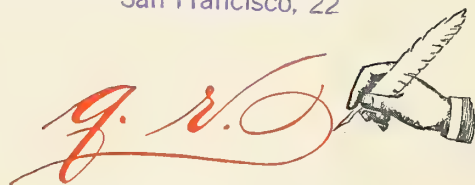


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ARIZONA MEDICINE

Journal of ARIZONA MEDICAL ASSOCIATION

VOL. 8, NO. 12



DECEMBER, 1951

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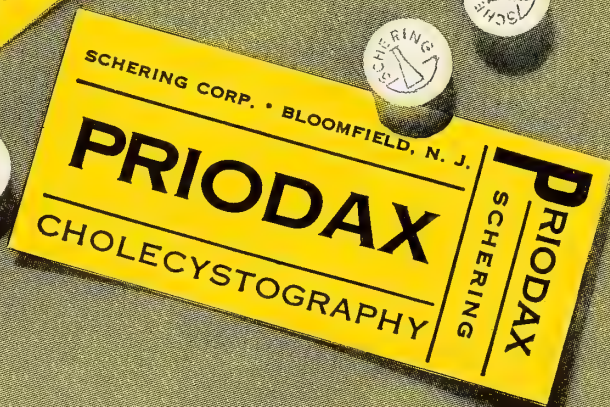
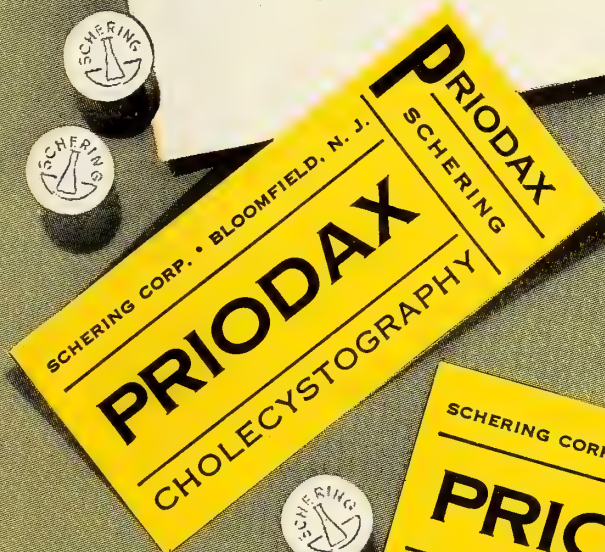
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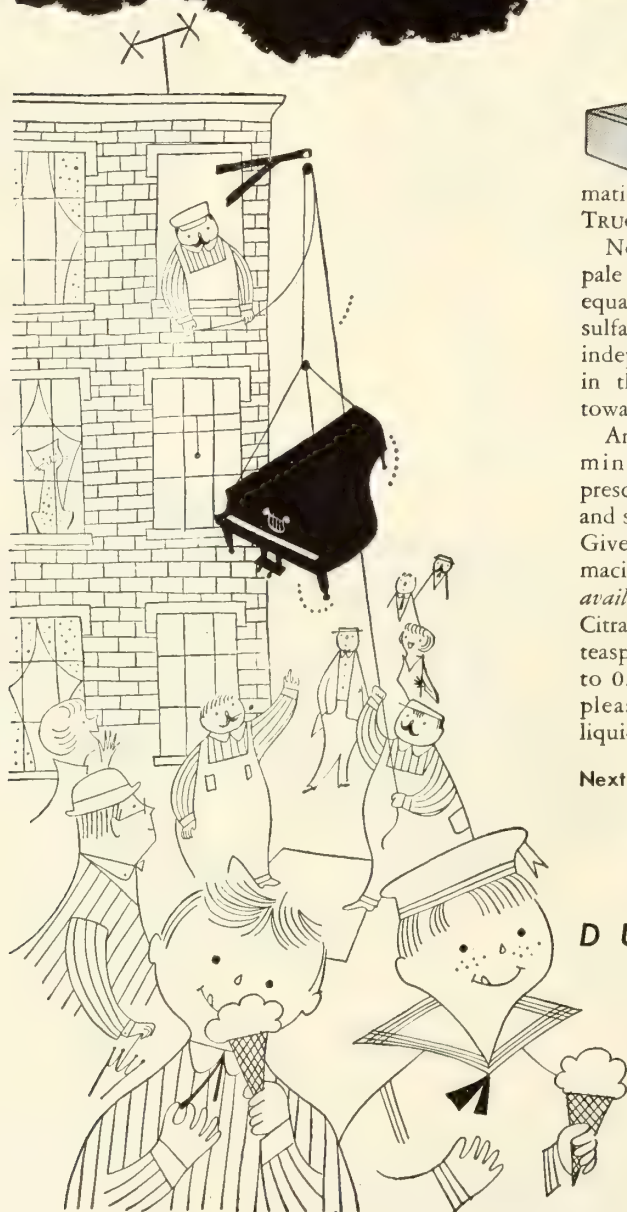
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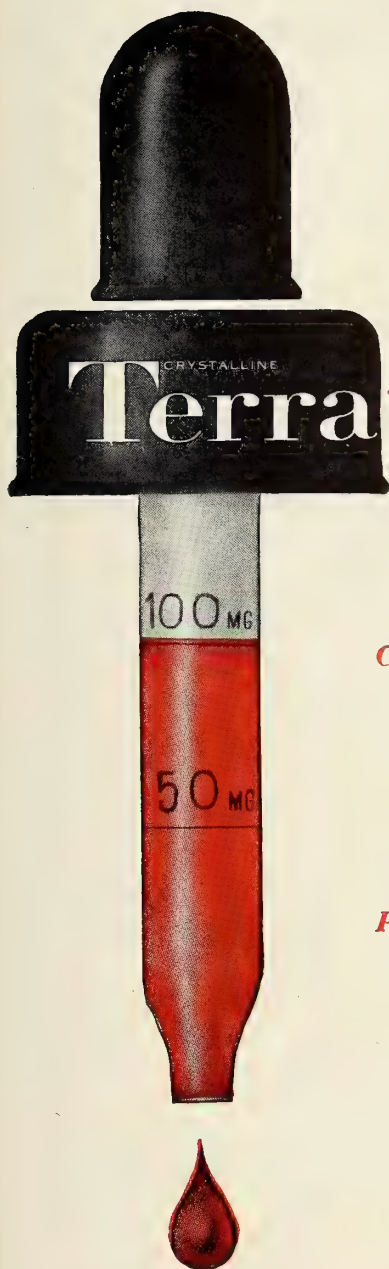
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*Gosselin, George A., M.D.
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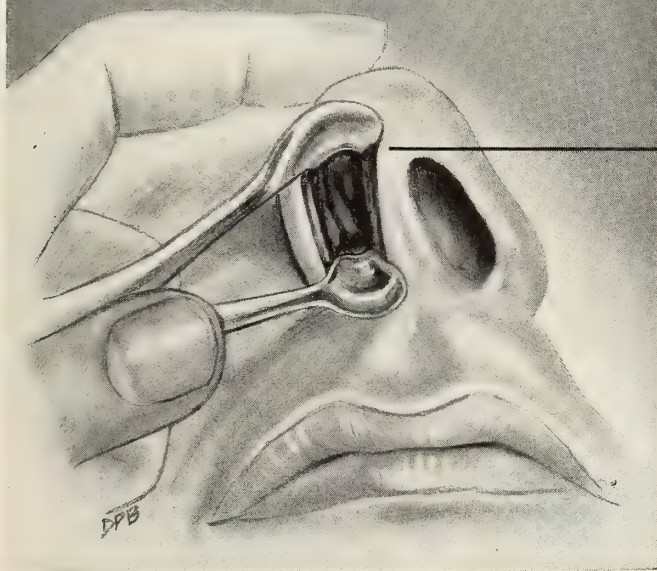


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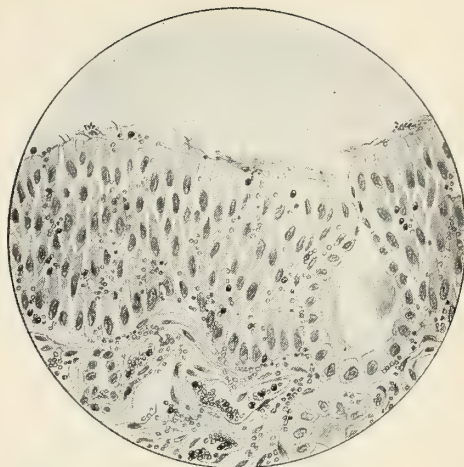
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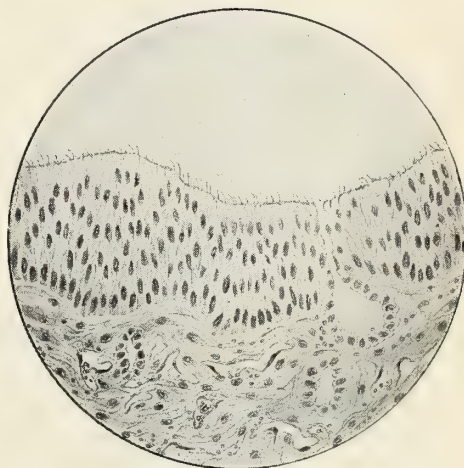
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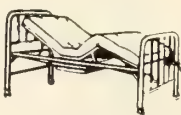


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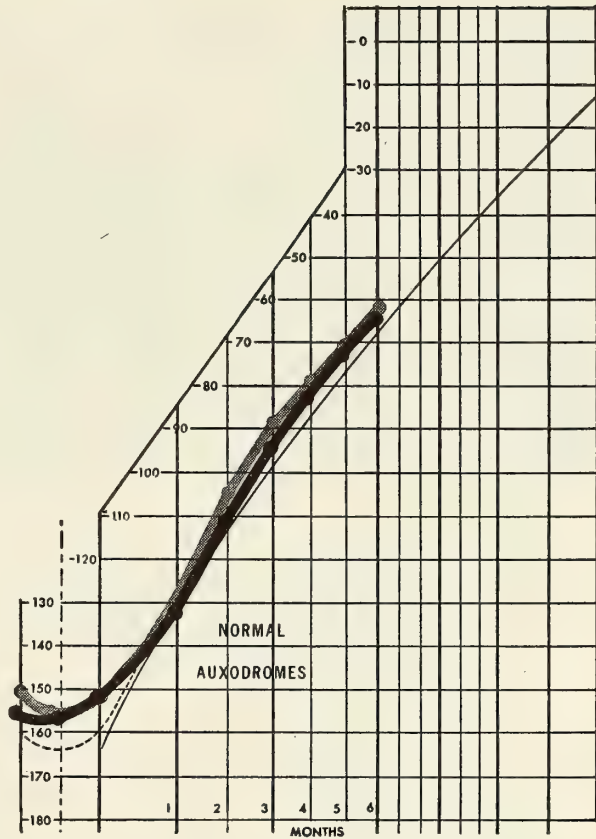
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Growth data, recomputed on Wetzel Grid, based on "selected subjects, most of whom were favored by environment;"² age: from birth to 6 months.

1. Wetzel, N. C.:
J. Pediat. 29:439,
1946.
2. Jackson, R. L.,
and Kelly, H. G.:
J. Pediat. 27:215,
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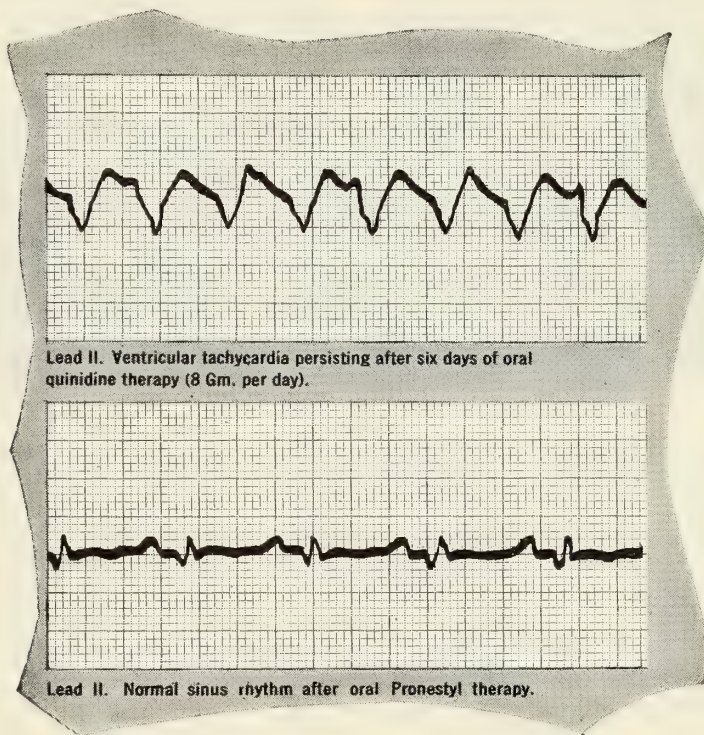
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Original ARTICLES

INDICATIONS FOR SURGICAL THERAPY IN EPILEPSY*

JOHN R. GREEN, M. D.

Phoenix, Arizona

Among the classic descriptions of diseases is the definition of epilepsy in 1866 by Hughlings Jackson(1):

"The term should be degraded to stand for our knowledge, or rather for our ignorance, of the various permanent and temporary conditions of nerve tissue in functional divisions, or perhaps in nutritive regions, which conditions cause or prevent temporary failures or losses of function."

Despite some progress, the inherent difficulties of the subject still create problems as to semantics, physiology and therapy.

For practical purposes, there are two major types of epilepsy: (1) Symptomatic, or acquired, and (2) Idiopathic, or cryptogenic. *Symptomatic epilepsy* includes focal and non-focal epilepsy of various types, which are secondary to known etiologic agents or lesions. Many of these patients with focal seizures should not be regarded as "epileptic," according to Walter(2). *Idiopathic epilepsy* includes non-focal seizures in which a cause cannot be surmised or found.

Therapy in epilepsy is primarily medical, with two exceptions,—namely: (1) Symptomatic seizures which are due to expanding intra-cranial lesions (i.e., neoplasms, abscesses, hematomata, etc.,) and (2) Chronic focal seizures of cortical origin which cannot be controlled satisfactorily with medications. The evaluation of these exceptional cases is discussed below.

DIAGNOSIS OF FOCAL EPILEPSY

The diagnosis of focal epilepsy is established

by answering two specific questions about each seizure problem: "(1) Where is the focus?, and (2) What is the cause?" (Penfield and Erickson(3).) The methods used to answer such diagnostic queries are a combination of (A) Clinical history and examinations, and (B) Laboratory examinations.

(A) *Clinical history and examinations:*

An accurate description of the aura and seizure pattern will provide the necessary information about the location of the focus of the initial "firing" of neurones, in many instances. This is particularly true of focal motor (Jacksonian) and various types of focal sensory auras and seizures. Epilepsy with "psychomotor" manifestations may indicate localization within the anterior temporal region or involvement of its subcortical connections. Generalized convulsions, without focal components, may represent initial "firing" from a "silent" functioning area of the cerebral cortex, but do indicate involvement of subcortical structures, directly or indirectly. Opisthotonic (decerebrate, cerebellar, tonic-postural) seizures usually mean that the pathology is affecting the brain stem. Minor seizures, of the triad described by Lennox(4), i.e., (1) brief lapses of consciousness (Petit Mal), (2) myoclonic jerks of the arms, and (3) sudden drop seizures, are believed to have a subcortical origin.

It is apparent that unless further evaluation discloses an expanding lesion, surgical intervention is considered only if *cortical* localization is definite, intensive medical therapy has been ineffective, and if there is some hope of rehabilitating the patient socially and economically.

*Presented at The Third Western Institute on Epilepsy, June 22-24, 1951, Salt Lake City, Utah.

From the Neuro-Surgical Unit of the Arizona State Hospital, and the Neuro-Surgical Service of Good Samaritan Hospital, Phoenix, Arizona.

Evaluation of the patient with the symptom, "epilepsy," is incomplete unless the cause of the disorder is investigated. The nature of the pathology which may be producing the seizures is frequently suggested by the age of the patient at the time of the first attack. For example, idiopathic (cryptogenic) epilepsy usually begins in the second decade of life. During the first two years of life epilepsy most commonly is caused by traumatic, degenerative, and congenital abnormalities. Febrile illnesses may create transient seizures and less commonly habitual attacks. When seizures start for the first time during childhood, birth injury, trauma during infancy, and occasionally febrile illness are the usual causes. Trauma and infantile brain injury may be the cause of seizures during the adolescent period, although lacking such history, the classification of idiopathic epilepsy is frequently necessary. From about 18 to 35, cerebral trauma most frequently precipitates attacks, and neoplasms occasionally. During the next twenty year period (35-55), the leading causes of seizures are: first, neoplasms; and then cerebral injury, and arteriosclerotic encephalopathy. From 55 to 70 years of age, the causes are the same with arteriosclerotic etiology becoming more frequent.

(B) Laboratory examination:

(a) *Electro-encephalography.* Important correlation of electro-encephalography and epilepsy began with the report of Gibbs, Davis, and Lennox(5), in 1935, that during a minor seizure (Petit Mal) the normal rhythm was replaced by 3/second wave and spike abnormality. Epilepsy has probably been studied more by EEG workers than any other condition since that time. Pioneer contributions in localization of brain tumors with this technique were made by Walter(6) as early as 1936. Although the EEG, like other laboratory methods, is not infallible, and is not specific for various types of pathology, it does indicate with a high degree of accuracy if abnormality is present and whether or not it is localized.

Clinical seizure patterns, which suggest stationary focal cortical disturbance, may show EEG features of localized abnormality. The commonest forms of such electrographic disturbances have been tentatively classified as follows (Walter (2)):

1. *Spikes.*
2. *Saw-tooth or square waves.*

3. *A combination of spikes and slow waves.*
4. *Slow waves.*

Localized spiking is commonly associated with clinical signs of cortical discharges and is generally regarded as indicating an "irritative" condition of the cerebral cortex,—the most reliable EEG evidence of focal epilepsy. Various methods of "activation" of the electro-encephalogram have been found useful to demonstrate these and other abnormalities,—such as, hyperventilation (Gibbs, Gibbs, and Lennox(7)), metrazol (Kaufman, Marshall and Walker(8)), Ziskind and Bercel(9), metrazol-photoc stimulation (Gastaut(10)) and sleep (Gibbs and Gibbs(11)).

(b) *Roentgenologic studies.* Plain films of the skull occasionally may indicate the location of the focus of the seizure disorder and its pathologic nature. Cerebral pneumography and angiography are frequently very informative in this regard and may be advisable if the location and cause of the epileptiform abnormality has not been ascertained by other methods.

THERAPY OF FOCAL EPILEPSY

Seizures, which are secondary to expanding lesions of the brain, require immediate neuro-surgical treatment. Focal epilepsy due to other causes should be managed satisfactorily with anti-convulsant medications, in the majority of cases.

I. Medical.

Medications are prescribed alone or in combination to the point of toxicity, including periods of prolonged sleep as described by Putnam(12). In general, seizures that follow cortical lesions respond to Phenobarbital, Dilantin, Mebaral, and Bromides, in approximately that order, and can be eliminated in more than 50% of the cases and decreased in another 25% of the patients (Walker(13)). Experimental drugs, not yet released, may improve these percentages. Surgical intervention has little point if the patient is so crippled physically or mentally as to have no chance for rehabilitation even if the seizures are stopped by surgery. It follows that no more than 20-25% of patients with chronic focal epilepsy become candidates for neuro-surgery.

II. Surgical.

The surgical treatment of focal epilepsy probably began in prehistoric times (Neolithic period of man in Europe and the era of the Peruvian Incas) with craniotomies to release evil spirits, including those thought to be causing epilepsy.

Directions for making a trephination on the side of the head opposite to a focal seizure were recorded by Hippocrates. Sir Victor Horsley's first craniotomy, on May 25, 1886, was for a cortical excision in a case of post-traumatic focal epilepsy,—a successful procedure.(14)

The remarkable work of Dr. Wilder Penfield and associates, since 1928 has indicated that 50% of the patients they have operated upon for focal epilepsy have been relieved, or almost relieved of attacks, and that another 25% of these patients were improved by the procedures (Penfield and Steelman(15)). Electrographic controls were added to the surgical armamentarium by these workers, in 1938, under the direction of Dr. Herbert Jasper. Refinements in these techniques have led to the observation that the role of the meningocortical scar is of less importance in the production of seizures than the pathologic cortex just adjacent to the cicatrix (Walker(16), Penfield(17)). Valuable data about the nature of the epileptic discharge has been obtained with electrocorticography. The tendency to direct the surgical extirpation by the use of the method alone has definite limitations (Meyers et al(18)), and, to date has not given appreciably better results than the simple removal of scars in instances of pathologic lesions (Bailey(19)). It is possible that as the applications of electrocorticography are better understood, the clinical results will improve.

The work of Fuster, Gibbs and Gibbs(20) suggesting that "psychomotor" seizures are focal in the anterior portion of the temporal lobe on one or both sides has created controversy as to terminology and concept, but has also stimulated intense investigative efforts, both in the clinic and laboratory. Experiences with anterior temporal lobectomy in cases of psychomotor epilepsy have been reported to show clinical results that are, to date, comparable with those obtained in the surgical treatment of other types of focal epilepsy (Bailey and Gibbs (23), 24), and Green, Duisberg and McGrath (21, 22).

Our observations(24) have led us to believe that the psychomotor seizure mechanism may involve a bilateral anterior temporal-subcortical circuit. These connections have been suggested in lower animals (Ajmone-Marsan, Stoll, and Jasper(25), and Hunter (26)), but have not been established in man. In psychomotor epilepsy, it would appear that an area of neuronal

pathology may fire this circuit in either direction, with local or generalized clinical and electrographic phenomena(24). It follows that clinical symptoms, signs, pathology and EEG abnormalities should be localized to the anterior temporal region, without evidence of major involvement of sub-cortical connections if surgical therapy of psychomotor epilepsy is to have maximal chances of success. More specifically, it has been observed that clinical states of rage, terror, fixed delusions, and psychotic abnormalities, in association with temporal automatisms and focal spiking on the EEG in the anterior temporal region, seem to indicate major involvement of subcortical structures, and have not been improved by anterior temporal lobectomy. Similarly, patients who manifest psychomotor states, focal pathology in the anterior temporal region, and at the same time show evidence of EEG dysrhythmia of subcortical origin are not considered to be satisfactory candidates for surgical intervention(24).

CASE REPORTS

Three cases are briefly described in order to illustrate some of the principles involved in the evaluation of epileptic patients for surgical intervention.

Case 1.

F. E., a 47 year old farmer developed a *generalized convulsion* on March 12, 1950. He had suffered no remarkable illness or injury prior to this date. There were no definite neurologic findings. Skull X-Rays were normal except for a slight increase in vascularity in the left fronto-temporal region. Electro-encephalography on March 17, 1950 was normal. Spinal fluid studies revealed an initial pressure of 250 mm. of water, and normal fluid findings except for a total protein of 63 mg.%. He was referred by Dr. Charles W. Sult, Jr. for neuro-surgical evaluation, with a tentative diagnosis of cerebral neoplasm, and admitted to Good Samaritan Hospital, Phoenix, Arizona. Ventriculography disclosed a normal ventricular system. Carotid angiography was done on the left side, the side of the questionable tortuosity of the vessels in the scalp and skull, and revealed a circumscribed area of dense staining in the left frontopolar parasagittal area. The tumor was removed and verified to be a *meningotheliomatous meningioma*, measuring 4.8 x 4 x 2.5 cm., (Fig. 1.) The patient recovered and has had no further convulsive seizures. His only handicap now is

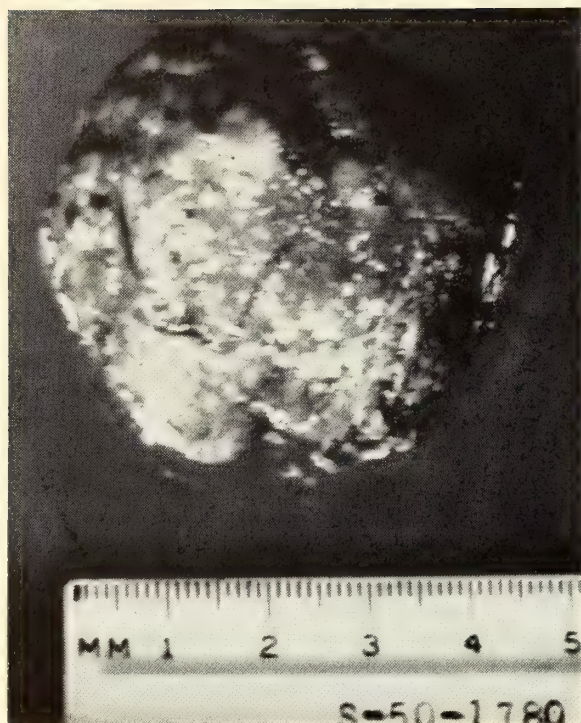


Fig. 1. Meningotheliomatous meningioma removed at operation. This benign tumor was the epileptogenic lesion in a patient who appeared to be normal except for convulsive seizures.

a mild osteoarthritis

The presenting complaint in this case, namely, a generalized convulsive seizure, was correctly surmised by the family physician to indicate so-called "symptomatic epilepsy" because of the age of the patient at the time of the first attack. Specialized neurologic studies did not reveal the cause of the episode until carotid angiography was done, which led to the successful removal of a benign neoplasm at the earliest possible time. Penfield and Erickson(3) have stated that epileptic seizures occur as the initial symptom in approximately 40% of all patients harboring cerebral neoplasms, and if seizures are the first symptoms of a space-occupying lesion, there is a two to one chance that the lesion is relatively benign.

Case 2.

A. O., a 34 year old Mexican housewife, was committed to the Arizona State Hospital on June 29, 1944, with the diagnosis "Epileptic Psychosis."

Early history was indefinite, but it was learned that she had had some type of generalized convulsive seizure at the age of 18 months, without recurrence until she was 10 years of age. The seizure pattern was characterized by mental confusion, a sensation of unreality and

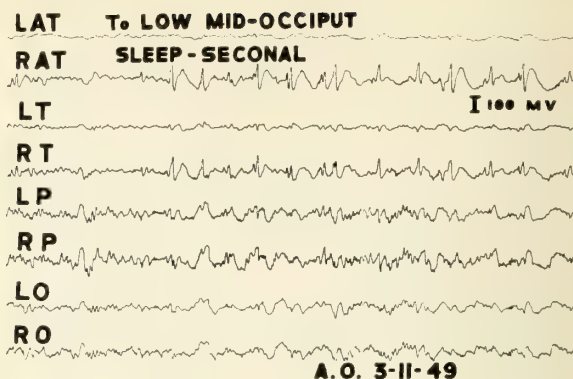


Fig. 2. Localization of right temporal lobe abnormality is confirmed by electroencephalography. Note the high voltage spike discharges in this area, maximal in the right anterior temporal region, during Seconal-induced sleep.

strangeness, staring, undressing, mumbling, chewing, formed visual hallucinations (lions, snakes), negativism, screaming, and occasional outbursts of violence and assaultiveness. She was treated with Dilantin and Phenobarbital, but it was eventually necessary for her family physician to have her committed to the Arizona State Hospital because of the increasingly frequent periods of violence and assaultiveness. It was noted that on admission to the hospital that she was calm, courteous and cooperative. The "psychomotor" seizures gradually increased, leading to suicidal and homicidal attempts, which created the necessity for caring for her on the disturbed ward most of the time.

The patient was referred to the Neuro-Surgical Unit of the Arizona State Hospital for evaluation. The following investigations were made:

(a) *Electro-encephalography* (March 11, 1949) disclosed the presence of a very active spike focus in the right anterior temporal-temporal area, confirming the clinical impression of temporal lobe (Psychomotor) epilepsy, and offering definite lateralization, (Fig. 2.)

(b) *Psychometric studies* (Wechsler-Bellevue Intelligence Scale), showed a verbal scale I.Q. of 54, performance scale I.Q. 67, and full scale I.Q. of 57.

(c) *Physical and Neurological examinations* were normal, except for arterial hypotension and poor oral hygiene.

(d) *X-ray studies of the skull* were normal, except for a metallic fragment in the soft tissues in the right temporal region. (No history could be obtained as to when and how this had occurred.)

(e) *Spinal fluid determinations* were normal.

(f) *Neuro-psychiatric examinations* was made

on August 10, 1949, by Dr. R. E. H. Duisberg. Her general attitude and behavior were marked by emotional lability, negativism, vivid facial expressions and gestures. The stream of mental activity was characterized by rambling digressions, hostility and vituperativeness. There was marked superficial lability of mood. Various studies of the sensorium (orientation, remote memory, immediate recall, counting and calculation, reading, writing, general intelligence, insight and judgment) revealed either complete or partial defectiveness. She was able to sing a little Spanish song of her own. The history of frequent severe outbursts of aggressiveness and assaultiveness during periods of clouded mental states was noted.

(g) *Pneumo-encephalography* disclosed normal ventricular and subarachnoid spaces.

These studies were considered to offer evidence of temporal lobe localization on the right side, with a suggestion that organic pathology would be found. The diagnosis of *Focal Epilepsy of Psychomotor Type (temporal lobe epilepsy)* was made, and, following consultation with Dr. F. A. Gibbs, Chicago, surgical intervention was decided upon.

Electro-corticography was done following a right fronto-temporal osteoplastic craniotomy and disclosed firing of high voltage negative spike discharges on the inferior surface of the third temporal convolution 2.8 cm. from the temporal tip, overlying a sharp osseous ridge.

Anterior temporal lobectomy (5 cm. from the temporal tip) followed. The surgical specimen appeared to be grossly normal. Microscopic study disclosed extensive hyperplasia of the pia-arachnoid, but no definite ganglion or glia cell abnormality.

The *post-operative* course was uneventful, marked by lethargy, but no aphasia, agnosia, or other neurologic changes. Within two weeks, she volunteered her services to help the nurses and attendants on the ward with mopping, cleaning and sorting linens and did these chores in a creditable manner.

Neuro-psychiatric evaluation on December 8, 1949, (REHR), 3 months following surgery, found decided changes, described below:

Her general attitude and behavior were much improved, being characterized by calm, neatness of dress, cooperation, pleasantness, and friendliness. The stream of mental activity had changed, and was not increased or markedly

retarded, and was without the previous tendency to rambling of thought and speech, and vituperative tirades. Some misrepresentations about herself persisted (i.e. reason for commitment.) She no longer had numerous somatic complaints or felt she was being annoyed. Her affect and mood were characterized by lability, pleasantness, alertness, and of giving the appearance she was going her best with her rather defective intellectual equipment. Various studies of the sensorium showed marked improvement. (Orientation was fairly correct, remote memory was well preserved except for some details, recent memory seemed fairly intact, she could repeat four figures forward and two in reverse, counting and calculation was not possible due to educational level. She was illiterate but could pick out a few words, she was able to write a little, low intelligence, but improved singing ability much improved, defective insight and judgment, but improved.) Her ward adjustment has been excellent post-operatively. On being called a "dirty Mexican" by a maniac patient, she took it well.

The last communication about this patient was received on May 21, 1951, 20 months following surgery, at which time there had been no recurrence of seizures or of behavioral outbursts, and the patient was reported by her mother to be making an adequate home adjustment.

This example indicates that good results may be obtained with surgical treatment in carefully selected cases of psychomotor epilepsy of severe degree under controlled conditions.

Case 3.

M. N., a 23 year old girl, was admitted to Good Samaritan Hospital, Phoenix, Arizona because uncontrollable convulsive seizures of Jacksonian type. Her birth and early development were normal, until she was six months of age, when she suddenly developed convulsive movements of the right hand, spreading to the extremity, side, becoming generalized. These attacks recurred every 3 hours for the next 24 hours and then stopped for a month, only to recur. During such a seizure, when she was two years of age, the intensity and frequency increased to status epilepticus, which was finally controlled at the end of one week. She was left with a paralysis of the right side of the body, mental retardation, and aphasic disorder. She gradually began to speak and to learn to use the left hand during the next year,

becoming ambulant again, but having a typical right hemiparesis. From this time to that of admission to the hospital the seizures would invariably begin in the right thumb and then involve the hand, occasionally involving the right side of the body, and less frequently becoming generalized.

A craniotomy was done elsewhere in 1936, when she was 8 years of age, but no evidence of chronic subdural hematoma was reported, and closure was made.

The child was tutored at home and learned well, although slightly retarded for her age. She was handicapped by the persistence of an infantile type of right hemiparesis, in addition to the focal (Jacksonian) epileptic seizures, which proved to be refractory to large doses of Phenobarbital, Dilantin, Mesantoin,—singly and in combination, and several periods of 72 hours of Barbiturate-induced sleep.

The patient was a brunette with considerable hirsutism. She cooperated well during the examination, spoke clearly, but showed definite evidence of slight mental retardation. There was a marked hemi-atrophy of the right side of the body, a right homonymous hemi-anopsia, and a moderate hemiparesis of the right side with most marked involvement and weakness of the right thumb. Sensation was intact, including stereognostic abilities. She was ambulant, but limped due to the right hemiparesis of infantile type. There was a well healed craniotomy scar in the left fronto-parietal region.

Electro-encephalography on January 11, 1951, showed an active spike focus associated with slow wave activity in the left mid-Rolandic area.

Pneumo-encephalography disclosed a huge porencephalic cyst in the left fronto-parietal region.

On May 19, 1951, the patient was anaesthetized with Sodium Pentothal, supplemented by Nitrous Oxide inhalation and 1% Procaine infiltration of the scalp. A generous incision was made circumscribing the previous one, preparatory to turning down a flap large enough to carry out hemispherectomy if necessary. The dura mater was adherent to the cerebral cortex in the mid-pre-Rolandic area, the extent of one gyrus. This gyrus was atrophic.

Electrocorticographic study (Fig. 3) revealed high potential 2-3/second activity from the cerebral cortex about the cicatrized zone, and spontaneous spike discharges from the gyri just

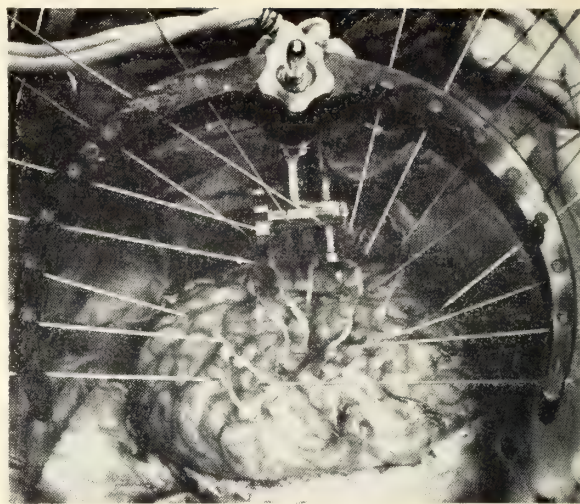


Fig. 3. Cortical electrode assembly (Grass) is clamped to calvarium and direct recordings are made from the accessible cortex (electrocorticography) to aid in the localization of an epileptogenic focus in a patient with unmanageable focal seizures (right hand) associated with a large porencephalic cyst. Note the area of microgyria in the mid-Rolandic region.

anterior and superior to the gross pathology.

It was not possible to accurately delineate the motor area by electrical stimulation.

Local cortical excision, utilizing subpial dissection methods as deep as the porencephalic cavity, was made not only of the atrophic area but also of the adjacent "firing" zone. It was felt that this procedure was less radical than a hemispherectomy, and that the latter procedure could be done later if the seizures were not controlled.

This patient illustrates a common form of focal motor (Jacksonian) epilepsy. The focus was well localized by the seizure pattern, neurologic examination, electro-encephalography and pneumo-encephalography. The pathologic nature of the lesion was suggested by the age of onset of the focal seizures, the hemi-atrophy, and pneumo-encephalogram. Although slightly retarded, she was not debilitated and could not be considered to be a social loss, except for the seizures. The seizures could not be controlled medically. These are the factors that are evaluated in each case prior to surgical intervention. A long term follow-up is required in all cases following cortical excision for focal epilepsy before the final results of such therapy can be evaluated,—a minimum of five years.

SUMMARY

The indications for surgical intervention in epilepsy must be strict, and include the following considerations:

1. Accurate diagnosis by clinical and labora-

tory methods must localize the origin of the seizure pattern to a single area of surgically accessible cerebral cortex, and indicate an epileptogenic lesion in this zone.

2. Symptomatic seizures which are secondary to expanding intra-cranial pathology, i.e., tumors, abscesses, hematomata, etc., require immediate neuro-surgical intervention.

3. Focal epilepsy which is secondary to chronic pathology, i.e., menigo-cortical cicatrices, microgyria, porencephaly, etc., should be managed satisfactorily with drugs in approximately 75% of the cases. Surgical therapy is indicated in patients of the group if intensive medical therapy fails, and if some degree of social and economic rehabilitation can be expected provided the seizures are stopped. The results of surgical therapy of focal epilepsy are generally satisfactory in approximately 50% of this selected group of cases, over a long term follow-up.

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SADDLE BLOCK ANESTHESIA IN OBSTETRICS

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Saddle Block Anesthesia is a type of anesthesia which is used extensively in obstetrical, rectal and genito-urinary work. As the name implies, it is anesthesia limited to the area coming in contact with a saddle. Pitkin(1), in 1928, appears to be the first American to describe this type of anesthesia, but it did not gain favor at first as it was not easily controlled and did not remain localized in the intended segments. It was, therefore, allowed to remain dormant until the early part of 1945 and 1946 when Adriani and Roman-Vega(2) published their work on Saddle Block Anesthesia and its control through the addition of glucose to the solution. With this work there was renewed interest in the subject.

We have the following comment from Parmley and Adriani(3): "The glucose inhibits dif-

fusion and, in addition, causes the solution to be hyperbaric or heavier than spinal fluid. When injected into the subarachnoid space with the patient in a sitting position, the solution gravitates downward and the drug becomes concentrated in the conus of the dural sac." Thus, the concentration surrounding segments higher than the saddle area is lessened, thereby decreasing the effect from complete anesthesia to analgesia. This gives definite relief of pain and sensation in the perineum, relaxes the perineal muscles and provides hypalgesia and analgesia over the legs and thighs without causing paralysis of the muscles of the legs and thighs. As the analgesia extends up to T10-T11 the sensory fibres of the uterus are affected and the pain of labor abolished.

Since the early part of 1947, one of us (PSC)

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has been using Saddle Block Anesthesia in Obstetrics, but it was not until January, 1948, that it was decided to use it routinely except where there were definite contraindications. We are presenting 1371 cases in which this type of anesthesia has been used, with complete success in all but three per cent of these cases.

The technique used in this series of cases is that first described by Parmley and Adriani(4) with some slight modifications as follows:

The Saddle Block tray is ready before the puncture is made. A 2 c.c. syringe is used and approximately 0.2 c.c. of Nupercaine(R) (1-200) is drawn into the syringe to rinse out the syringe before preparing the solution for injection. This is very essential as the Nupercaine(R) solution is precipitated by the slightest amount of alkali. Following this, 0.7 c.c. of Nupercaine(R) is drawn into the syringe and to this is added 1.3 c.c. of 10% glucose to make a total of 2.0 c.c. solution. The syringe is then placed on the tray for usage after the lumbar spinal puncture is made. The lumbar spinal puncture is made in L3-L4 with a 22 or 20 gauge needle with the patient lying on her side. When a steady, clear flow is obtained, the syringe containing the Nupercaine(R) solution is connected to the spinal needle. A slight amount of spinal fluid (0.1 c.c.) is aspirated to determine that the needle is still in position and then the content of the syringe is injected at the rate allowed by the needle. The patient is then immediately turned on her back and placed in a sitting position with the legs extended for 25 to 30 seconds, then allowed to return to a supine position with two pillows under her head and shoulders. The anesthetic usually starts to take effect immediately and the patient becomes comfortable. The injection must be made between contractions because the spinal fluid pressure is increased at the time of contraction. Currents established in the sub-arachnoid space during a contraction force the drug into the thoracic region, giving greater distribution of anesthesia and halting labor.

The Nupercaine and glucose is now available in a 2 c.c. ampule which contains 5 mgm. of Nupercaine. This preparation is known as "Heavy" Nupercaine(R)* and we have substituted it for our previous technique of mixing Nupercaine(R) 1-200 with 10 per cent glucose. In using a pre-mixed ampule the entire content

is used, after first rinsing the syringe to eliminate the alkali.

(* "Heavy" Nupercaine was furnished through the courtesy of Ciba Pharmaceutical Products.)

One of the changes from the Parmley-Adriani technique is the position used for the lumbar puncture. We have found that there is very little difference, if any, in the level of the anesthesia if the change in position is achieved within 2-3 seconds. One of us (WAR) used the sitting position on the delivery table and the other (PSC) the side position until we could see no difference, and now the side position is used entirely.

Another change is in the dosage. It is apparent that a larger dose has been used in this series.

A third change is to be noted in the length of time the patient is allowed to remain in the sitting position.

The total effect of these latter two modifications of the Parmley-Adriani technique is to raise the level of anesthesia to T-10 in most instances and increase the anesthetic effect. It is our clinical impression that these changes were necessary because of the type of individuals presenting themselves for delivery by this technique in private practice. These patients demand that they feel no pain. Many of the cases mentioned below which required supplemental anesthesia occurred early in the series, at which time the Parmley-Adriani technique was strictly followed. Since the dosage and level have been altered as above, very few patients have required supplemental anesthesia.

The ages varied from 16 to 42 years and the primipara and multipara were about evenly divided. The premedication was decreased somewhat and total dosage usually averaged seconal, grs. 1½; demerol, 150 mgm.; and scopolamine, grs. 1/100. When the primipara were about 8 cm. to complete dilatation the Saddle Block was given. In the multipara, the Saddle Block was given when there was 6-7 cm. dilatation of the cervix.

Saddle Block Anesthesia was discussed with the patient by the attending physician during one of the routine office visits. An attempt was made to answer all questions in order that the patient came to the delivery table in readiness for the block. It should be emphasized that the term "Saddle Block" must always be used

and the word "spinal" avoided as much as possible.

The block usually becomes effective within 2-5 minutes, but in some cases several contractions were experienced before complete relief was obtained. In one case, the block was given in bed and the patient was not relieved of labor pains although the head of the bed was tilted to a slight degree. After a few minutes waiting, it was thought best to take the patient to the delivery room and repeat the block under more ideal conditions. On arrival at the delivery room (about 15 minutes after injection) the patient was again tested and the anesthesia found to be complete, hence we are now willing to wait 10-20 minutes before repeating the block on an apparent failure as there are some few cases in which the anesthetic takes longer to become effective. The reason for this is not clear.

From the time of the injection of the anesthetic agent until the arrival of the patient back into bed after the delivery, all of the patients were able to move their toes and could assist themselves, but commented that they could not tell where their feet were and that the buttocks felt heavy.

There was a slight drop in the blood pressure in the majority of the cases, averaging approximately 10 mm. of mercury in the systolic and very little, if any, in the diastolic. About 5 per cent of these cases required a vasopressor drug. These drugs are routinely given in any case where the systolic drops below 90 mm. of mercury: Oenethyl (50 mgm., intramuscularly or intravenously, depending on the response desired); or Ephedrine, 50 mgm., given in a similar manner, or Neo-synephrine, min. III, intramuscularly. At the beginning of the series, ephedrine, 50 mgm., was used in the skin wheal, but this was stopped as the patients often complained of severe headaches of 5-10 minutes in duration shortly after the start of the anesthetic. This complaint ceased after the use of ephedrine was discontinued. Now there is no skin wheal made, and the initial puncture with the spinal needle is made when a contraction is present. In four cases it was necessary to give a second dose of vasoconstricting agent, and two cases required the administration of intravenous fluids to maintain the blood pressure at a satisfactory level.

Nausea is still present in some of the cases, but it is seldom considered to be due to the anes-

thetic. Investigation is now being carried on to see if it is not due to the ergotrate-like drugs used during the delivery, since nausea is most frequent after the ergotrate which was administered intravenously at the time of the delivery of the head. The contractions were slowed for a short period of time in some instances, but these soon returned to normal rhythm without further medication. It was believed that the strength of the contractions was diminished in most cases.

Headaches were encountered no oftener than in the usual spinal tap cases. There were only five cases in which there was a true, severe, "spinal headache," and these lasted from 2-3 days. A one-pound sand bag is routinely placed on the abdomen against the uterus and the patient's head is raised slightly. This procedure has seemed to decrease the incidence, but has not done away with the headache entirely.

In this series, low forceps and episiotomy was the routine, but approximately 75 of the cases had spontaneous deliveries. Some few complained of a light, tugging feeling, but usually the mother was not aware that the baby was born until she heard it cry. It is most gratifying to hear the comments and to see a mother's face when she realizes that her delivery is over and she has had so little pain.

The reported duration of anesthesia in 1028 cases, from the time the block was given until the patient returned to bed after delivery with satisfactory anesthesia throughout, can be tabulated as follows:

76 cases	½ hour or less
461 cases	½ hour to 1 hour
304 cases	1 to 1½ hours
100 cases	1½ to 2 hours
53 cases	2 to 2½ hours
20 cases	2½ to 3 hours
10 cases	3 to 4 hours
1 case	4 hours
3 cases	4½ to 5 hours
1 case	10 hours

Saddle Block was repeated in 24 cases. There was no maternal or infant mortality in the series that could be attributed to the anesthetic or technique of administration.

Adriani explains the occasional complete failure as being due to faulty technique. Apparatus for the administration of oxygen and artificial respiration was always at hand for any emergencies. Oxygen at 5 litres per minute is usu-

ally given to the mother as the delivery starts, but no other measures were found necessary.

In a few recent cases, where the patient complained of the anesthetic wearing off after the delivery has started, we have given sodium pentothal intravenously instead of repeating the block. When sodium pentothal anesthesia is used everything must be ready to complete the delivery, as no more than eight minutes may pass before the infant shows signs of pentothal anesthesia. We prefer that the delivery be accomplished in less time than this, however. It is rare that more than three minutes elapse between the start of pentothal and the clamping of the cord. With the small dosage of pentothal required, the mother is usually awake before the episiotomy is completely repaired. There is no discomfort during the repair procedure as the block anesthesia is still present in the perineum.

This type of anesthetic is very satisfactory in obstetrics. It is, of course, not yet the perfect anesthetic for obstetrics. We believe that it will give the best results for mother and child. The simplicity of the technique and ease of the administration are major factors in its favor. The simplicity means it is an anesthetic suitable for use by the small town practitioner. However, a warning must be given that it is to be used cautiously, and the pitfalls must be fully understood before putting it into practice.

Unusual incidents occurring in some of the cases were:

1. One patient had a massive uterine hemorrhage, requiring immediate blood transfusion, which was unrelated to the anesthetic.

2. One patient had a mild eclamptic convulsion one minute after the anesthetic block, starting while patient was in the sitting position. The delivery was quickly completed following the cessation of the convulsive movements. Oxygen was administered during an uneventful delivery and the patient returned to her bed in good condition. Another convulsion occurred in 45 minutes following return to the

room and another one in 15 minutes. Following this, the patient had an otherwise uneventful postpartum. It is believed that this patient was a borderline eclamptic, and the added amount of ephedrine was just enough to cause the patient to become eclamptic with the above manifestations.

3. One case had a severe headache accompanied by transitory hypertension during and immediately following delivery with relief within an hour as pressure declined.

4. One case had pain during the delivery of the head although the skin anesthesia level was at T10.

In this series of 1371 cases, additional agents were needed due to the expiration of anesthesia or other causes as listed below:

Nineteen cases were given pentothal for delivery of head (16) and extractions of stillbirths (3).

One case was given chloroform for manipulation of a transverse position to a breech with extraction.

Eight cases were given nitrous oxide and oxygen for delivery of the head.

One case was given ether for the delivery.

One case was given pentothal, oxygen and ephedrine for nausea and a fall in the blood pressure.

SUMMARY

Saddle Block Anesthesia is not a new anesthesia; it has been known since 1928. It has been reintroduced for use in obstetrics.

A technique with Nupercaine(R) 1-200 and 10 per cent glucose, and the anesthesia with the newer, pre-mixed "Heavy" Nupercaine(R) is described.

The analysis of 1371 cases of Saddle Block Anesthesia shows that it is a safe, desirable anesthesia in the hands of qualified personnel.

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INFANTILE CORTICAL HYPEROSTOSIS

A Report of Two Cases

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In 1945 Caffey and Silverman described four cases of infantile cortical hyperostosis,(1) a syndrome characterized by, onset during the first four months of life, tender swellings deep in the soft tissues and, cortical thickenings of the skeleton. This article was followed in 1946 by another by Caffey(2), as well as one by Smyth, Potter, and Silverman(3), describing similar cases. Since then articles have appeared adding other cases. (4, 5, 6, 7, 8, 9). If the diagnosis be limited by strict adherence to the above triad of criteria plus a fourth later added by Caffey(10), namely, that the mandible must be involved in the process, the total number of authentic cases still is only between two and three dozen. It is the purpose of this paper to present two additional cases, which fulfill all criteria, except that the onset in one case was apparently during the sixth month, and to review briefly the characteristics of the syndrome.

Case I.

P. B., female was born September 1, 1948. Birth weight was five pounds, ten and a half ounces. The pregnancy and labor were normal. The child developed normally for two months, but at the age of three months when she weighed ten pounds, seven ounces, it was noted that she had a purulent left otitis, that her head was asymmetrical, and that she showed definite craniotabes. She had been on five drops of Navitol (R), a vitamin A. and D. preparation since one month of age. Infron (R) capsules, each containing 100,000 U.S.P. units of water dispersible vitamin D. were prescribed, one capsule to be given each month to facilitate the disappearance of the craniotabes. Despite written instructions to the contrary, the mother gave all six capsules of Infron within a period of six days. During the next three months the child was seen five times, on four of which there were signs and symptoms of respiratory infection and mild left catarrhal otitis. Weight gain during this period was three and a half pounds—somewhat less than average. On March 1, 1949, at six months of age, the child was reported to be eating poorly and to be "biting on everything."

Physical examination was not remarkable, and though subsequently the mother stated she thought the swelling started prior to March 1st. at this time no swelling of the jaw was noted. Three weeks later, however, on March 22nd the same symptoms were reported, and she had lost one ounce in weight. At this time she had 100.2 temperature by rectum, and there was definite swelling of both jaws. Infantile cortical hyperostosis was suspected, and confirmed by X-ray of the mandible, (Fig. 1) which showed periosteal reaction and new bone formation about the mandible. X-ray study of the complete skeleton showed no other involvement. The urine was normal. The hemoglobin was 9.5 grams, erythrocytes 4.4 million, leucocytes 22,650, with a normal differential count. The child was tried on a course of a triple sulfonamide preparation for several days, and during the next eight days gained six ounces. However, the jaws seemed to increase in size. Elixir of Pyribenzimine(R), 3 teaspoons a day, were prescribed for a two week period. During this time the child cried hardly at all, ate better, and continued to gain. The swelling of the jaws seemed to diminish. Follow up x-rays taken on May 6, 1949 showed the laminated periosteal reaction previously demonstrated was considerably less apparent than on 3-23-49 though there was probably some slight increase in density of the mandible. The frontal projection showed some increase in width of the mandibular hami. There appeared also to be residual soft tissue swelling about the mandible though it was somewhat less than previously demonstrated. Though clinical symptoms had disappeared, the periosteal reaction with resulting new bone formation was still present. Following a communication from Dr. Caffey of New York, the administration of Navitol(R) was discontinued for two months. From then on the child continued to improve, the jaws grew progressively smaller, and by July 27th were felt to be within normal limits. Growth and development continued slightly below average. On December 6, 1949, at the age of fifteen months, the child weighed nineteen pounds, six ounces, and was slightly anemic, the hemoglobin



Fig. 1. Case I. Lateral Roentgenogram of the mandible at six and one-half months of age, two weeks after appearance of facial swelling. Horizontal rami show laminated periosteal reaction and new bone formation resulting in diffuse increase in volume of bone and sclerosis. There is no destruction.

being 10.8 grams. In other ways, however, development was normal. The child has not been seen since that date.

Case II.

P. C., male was born November 12, 1950. Birth weight was six pounds, seven ounces. Pregnancy, labor, and delivery were normal. The child was breast fed for five weeks, and then put on a routine evaporated milk and Dextri Maltose (R) formula. Abdec (R) 3/10 of a cc. daily was commenced at the age of one month. The child was first seen in the office on January 10th at two months of age, weighing nine pounds, three ounces, with a complaint of fever and diarrhea. Sulfadiazine was prescribed. The fever disappeared, but not the diarrhea. One week later the child was placed on boiled skim milk, aureomycin, and later streptomycin. On February 1st the weight was ten pounds, two ounces, and the child was having two very loose stools daily. Culture of the stools showed *Salmonella*. Over a period of the following two weeks the diarrhea gradually ceased. The child was next seen on March 6, 1951 at the age of four months, with a complaint of swelling and tenderness of the left parotid area. Rectal temperature was 102 degrees. This was tentatively



Figure 2. Note swelling of jaw.

diagnosed as mumps, and aureomycin was prescribed. Six days later the firm, very tender swelling had extended to include both sides of the face. (Fig 2) The liver was slightly enlarged. The hemoglobin was 8.5 grams, the erythrocytes 3.8 million, leucocytes 16,100, with a normal differential. Penicillin was prescribed as a non-specific infectious parotitis was suspected. Four days later the swelling was still present, and infantile cortical hyperostosis was diagnosed. X-ray examination on March 21st (Fig. 3) showed double cortical margins of the inferior cortices of the horizontal rami of the mandible. Some soft tissue swelling in parotid and submaxillary regions was apparent. Though the density of the mandible was only slightly increased, and the usual laminated appearance was not obvious, it was felt that this was infantile cortical hyperostosis involving the mandible. X-rays of the remainder of the skeleton showed no further involvement by the disease process. In the six weeks following diagnosis the child gained normally and the swelling slowly diminished, though on April 24th the mandible still felt enlarged. Tenderness had disappeared by



Fig. 3. Case II. Roentgenogram of the mandible at four months of age. There is laminated new bone formation with diffuse thickening and sclerosis together with soft tissue swelling. Mandibular involvement has been present in all cases reported to date.

April 24th. X-ray on that date showed slight improvement in the process.

DISCUSSION

Both these cases have certain features in common. The disease appeared between the ages of four and six months. Both children had a low grade fever, leukocytosis, with normal differentials, and a tender painful swelling of the face, which failed to respond to antibiotic therapy. In each case there was a preceding history of infection. In the first the infection was upper respiratory with otitis; in the second *Salmonella* enteritis. The first case was complicated by the inadvertent administration of 600,000 units of vitamin D. within a period of six days. This administration was approximately three months prior to the clinical diagnosis of hyperostosis, and its significance is doubtful. In both cases the child made an uneventful recovery. In the first case the improvement incidental to the administration of an antihistamine is of interest, but doubtful significance.

The etiology of the disease remains obscure. There is, however, a growing mass of evidence which effectively excludes many possibilities. During the course of investigation by various authors, such things as syphilis, tuberculosis,

blood dyscrasias, scurvy, rickets, hypervitaminosis A., typhoid, paratyphoid, Brucellosis, bacterial, ricketsia, or viral infection, and allergy have been excluded by laboratory tests or therapeutic failures, as possible etiological agents. Hypervitaminosis D. particularly interested us in view of our first case, but search of the literature on the subject fails to reveal any confirmation that large amounts of vitamin D. can produce the syndrome. Hypervitaminosis D. results in a generalized osteoporosis and metastatic calcifications occurring in almost any organ or tissue of the body, but especially frequent in the periarticular structures(11). This is quite a different roentgenologic picture from that described in infantile cortical hyperostosis.

It has been speculated that hyperostosis in the early age group may represent an unusual reaction to infection, and the low grade fever and leukocytosis may be advanced to support this theory, which remains, however, still unproven. Infection apparently preceded the hyperostosis in only seven of twenty-three cases reported in the literature.

Caffey has recently asserted that the age of onset is invariably during the first four months of life, one case having shown typical signs on the first day of life.(10) Our first case probably started during the sixth month, and there seems no reason to doubt that cases may commence this late. There is no predominance of either sex. The presenting symptoms are usually irritability, fever, and a brawny swelling of the face. There was a striking similarity in the facial appearance of our two cases and, indeed, they resembled the pictures of the other patients so much that all could be siblings.

The fever is variable, though usually low grade. It may subside in a few weeks or persist for months. The irritability seems to be due to the pain experienced when the affected parts are moved. When undisturbed, the babies usually remain placid and content. The areas of actual swelling are quite tender, necessitating only a slight stroking of the skin to produce a cry of pain.

The site of the soft tissue swelling is usually that of the cortical hyperostoses, and as these vary from place to place in the individual there is no uniformity as to their location, with the exception that the jaws are always involved. Small hyperostoses may occur without the presence of soft tissue swelling. The soft tissue

swelling may be present for some time before the bony involvement is noticeable, and roentgenographically may appear in successive new sites, while the earlier swellings in another site are disappearing. There may be one or more recurrences of the swelling occurring as long as several weeks after their initial disappearance. Recurrences tend to be milder and of shorter duration than the initial occurrence. Bony lesions persist long after external signs and symptoms have disappeared.

The cortical hyperostoses are most commonly found in the mandible, clavicle and ribs. Other sites include the scapula, calvarium, and all the tubular bones, excluding the phalanges.

The basic roentgen change is an external thickening of the cortex, which in many instances was laminated, giving an onion peel appearance. The external margins of the cortical swellings are irregular. These cortical thickenings do not extend the entire length of the bone, but leave the terminal segments of the shaft unaffected. The spongiosa, the metaphyses, the epiphyseal plates and ossification centers in the epiphyses all are normal. Biopsy of the bone disclosed only hyperplasia of normal lamellar bone.⁽⁶⁾ There was no evidence of old or recent inflammatory changes, nor were subperiosteal hemorrhages present. Muscle biopsies showed some vacularization and degeneration of muscle fibres with brosis.

There is usually a leukocytosis ranging from 12,000 to 28,000. Some authors report a moderate increase in lymphocytes, others a polymorphonuclear reaction. A moderate increase in sedimentation rate is usually found some time during the course of the disease. Blood calcium, phosphorus and phosphatase levels have not varied consistently or greatly from normal.

Differential diagnosis of the swelling includes mumps, infections and neoplasm of the parotid glands, and leukemia. The irritability is suggestive of scurvy. The lesions of the bones suggest osteomyelitis or neoplasm. The most common error occurring in the literature, as was the case in Caffey's two earlier articles, (1, 2) was the inclusion of cases occurring after the twelfth month of life. These Caffey now believes to be hypervitaminosis A. This latter condition does not show mandibular involvement or fever and does have increased vitamin A. levels and frequent metatarsal hyperostoses, whereas the opposite is true in in-

fantile cortical hyperostosis. It is well known that the giving of excessive vitamin concentrate during the first four months of life has not produced the manifestations of infantile cortical hyperostosis. Indeed, from the proven cases of hypervitaminosis A. it was apparent that the vitamin must be given not only in large amounts, but also over a prolonged period of time in order that the syndrome be produced.

Treatment of infantile cortical hyperostosis is at the present writing largely expectant. Sulfonamides and antibiotics have been unsuccessful. The apparent good results with pyribenzamine (R) in our one case were not confirmed when Benadryl (R) was tried in others, in the literature. Specific therapy must probably await demonstration of the true etiology. Recovery with disappearance of all swelling within a few months is the rule.

SUMMARY

Two cases of infantile cortical hyperostosis, involving the mandible have been presented. Hypotheses regarding etiology and the characteristics of the disease have been discussed.

Since this article went to press a third case involving only 1 side of the mandible has been studied by us.

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GALLBLADDER SURGERY AT ST. JOSEPH'S HOSPITAL A STATISTICAL AND COMPARATIVE REVIEW

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In reviewing all gallbladder surgery in a private hospital performed in the year 1950, it occurred to the author that it might be of general interest to compare such a study with statistics from a large well-recognized hospital or clinic group. A search of the literature revealed few articles concerning a comprehensive survey of gallbladder surgery, although there was a great variety of articles covering certain details or aspects of gallbladder surgery. Fortunately an excellent review was found from the Lahey Clinic to serve as a basis of comparison. This was an article by Adams and Stranahan entitled "Cholecystitis and Cholelithiasis, an Analytical Report of 1,104 Cases," appearing in *Surgery, Gynecology and Obstetrics*, Volume 85, Page 776, 1947. The reader is referred to this article for details and a most comprehensive bibliography. For the purposes of this paper the format will follow closely that used by these authors.

ETIOLOGY

The review of this series of gallbladder cases contributes nothing to the etiology of gallbladder disease as we now know it.

INCIDENCE

During the year 1950, 121 patients were operated at St. Joseph's Hospital, Phoenix, Arizona, for various types of gallbladder disease and with various types of operative procedures. Of this group 92 (76 per cent) were between the ages of 31 and 60. Of the Lahey group 831 (75 per cent) were in the same age group. The youngest patient operated at St. Joseph's Hospital was 18 years of age as contrasted with a patient 9 years of age operated at the Lahey Clinic. In both series the oldest patient was 81 years of age. The average age of the St. Joseph's group was 47.5 years; the Lahey group did not state an average.

Twenty males and 101 females were operated at St. Joseph's. This is a ratio of approximately 1 to 5. The ratio of the Lahey group was 1 to 3. The race incidence was 120 whites to 1 colored. This incidence is statistically of no significance.

The average stay in the hospital of this group

of patients was 12.1 days. The shortest stay was 6 days; the longest 66. The average number of postoperative days was 9.9. The shortest postoperative course was 4 days; the longest 29. The longest stay and longest postoperative course occurred in an elderly male who was admitted for an acute coronary thrombosis and developed an acute gangrenous cholecystitis while in the hospital for that disease.

Using the highest temperature as an index of morbidity, the average highest temperature was 101.3 degrees F. The average day on which this highest temperature was reached was 2.1 days. There are no comparable figures in the Lahey report.

SYMPTOMS AND SIGNS

Symptoms were present in 3 cases for 20 years. The shortest duration of symptoms was 1 day occurring in 2 cases. The average duration of gallbladder symptoms of all types in all cases was 20.7 months. In 22 cases the exact duration of the disease was not specified in the history. One patient had had a previous cholecystostomy 7 years prior to surgery, and another 15 years prior to surgery. The history was refused the intern in 1 case.

JAUNDICE

Twenty-three patients (19 per cent) gave a history of previous jaundice or were jaundiced on admission. This compared with 18 per cent in the Lahey group. Sixty-two patients (51 per cent) denied jaundice and other obstructive signs such as dark urine and alcoholic stools in the past. In the history of 36 patients, obstructive signs were not mentioned. Five patients had common duct stones proven by operation; three gave a history of jaundice, 2 did not. Common duct stones were not found at operation in 18 of the 23 patients giving a history of jaundice. Adams and Stranahan state in their report that "200 patients gave a previous history of jaundice or had jaundice on admission to the clinic. Jaundice was present in 95 (51 per cent) of the 186 cases in which common duct stones were removed, and in 105 (52 per cent) of the jaundiced cases common duct stones were not found at operation. One hundred eighty-six

had proved common duct stones, but almost one-half (89 or 47.8 per cent) of these patients with common duct stones did not have jaundice." In the St. Joseph's group 3 patients underwent common duct exploration in whom jaundice was denied and in whom no stones were found. One case in whom jaundice was not mentioned in the history revealed no common duct stones on exploration.

PHYSICAL FINDINGS

The group under consideration was described as completely negative on abdominal examination in 29 or 24 per cent of the cases. Tenderness in the right upper quadrant was elicited in 91 or 75 per cent. A palpable mass was definitely described in 6, a questionable mass in 4, and no mass in the gallbladder region was described in 111 cases. This is consistent with the postoperative diagnosis of only 9 acute cases since a chronic retracted gallbladder would hardly be expected to be palpable. Enlarged liver was described in 2 cases, jaundice in 2 and an elevated icterus index was found in these 2 patients.

ROENTGENOLOGIC EXAMINATION

Oral cholecystographic examination of the gallbladder was done prior to surgery in 91 or 76 per cent of the 121 cases. In 1 case cholelithiasis was discovered during the exploration at a previous operation. In the histories of 29 of our patients cholecystography was not mentioned. The Lahey group had cholecystography in 92.4 per cent of the cases. A correct radiological diagnosis was made in 85 or 82 per cent of the present series. This compares with a correct diagnosis of 98 per cent of those in the Lahey group having radiological examination prior to surgery. The number of patients actually having X-ray studies in this series was probably higher, but was not mentioned by the intern in taking the history. The correctness of diagnosis would also probably be higher accordingly. In 52 of our patients (57 per cent) stones were visualized, comparing with 62 per cent of the Lahey Clinic group. Non-functioning gallbladder was described in 24 cases (20 per cent), a poorly functioning gallbladder in 2, reduplication of the gallbladder in 1, and in 12 histories X-ray studies were mentioned but conclusions were not specified.

OPERATIVE TECHNIQUE

A vertical incision was employed in 51 per

cent of the series studied, some modification of the subcostal or transverse incision in 48 per cent, and a Mayor incision was used in 1 case.

Penrose drainage was used in 76 or 62 per cent of our cases. T-Tube drainage was employed in 8 and a small urethral catheter drain in 8. The wound was closed without drainage in 30 or 25 per cent of the cases studied, but in each such case hemostasis was described as being practically complete.

OPERATIVE FINDINGS

Adhesions were described in 56 or 46 per cent of our cases. Cholelithiasis was proven by operation in 85 or 70 per cent. Common duct stones were found in 5 cases, a gangrenous gallbladder in 2, cirrhosis of the liver was described in 2, hydrops of the gallbladder in 1, and the gallbladder was not described in 2 cases.

SURGICAL ACUMEN

Table I shows the various preoperative, postoperative and pathological diagnoses.

It is to be noted that the term "lymphocytosis" employed in this table signifies the description on the part of the pathologist of "focal areas of lymphocytes" which for all intents and purposes is a diagnosis of a normal gallbladder. It is to be kept in mind however, that other conditions may be present producing gallbladder symptoms than an out-and-out anatomical disease of the gallbladder as such. For instance, cholecystic dyskinesia has no pathological counterpart and a gallbladder removed in such a condition would not necessarily show any pathological changes. However, cholecystectomy would cure a patient suffering with such a diagnosis. Similarly, cholesterosis would be a purely pathological diagnosis unless the surgeon wished to confirm his preoperative and postoperative diagnosis at the time of operation by opening the gallbladder himself. The lack of confirmation of choledocholithiasis by the pathologist is fallacious since the pathologist presented only with stones as such would have no way of knowing their origin. No direct conclusions may be drawn from this table except that one gets the impression from a study of it that the preoperative, postoperative and pathological diagnosis in this series of patients correlates with a fair degree of accuracy.

OPERATIVE PROCEDURES

Cholecystectomy alone was performed in 107

TABLE I

<i>Diagnosis</i>	<i>Preoperative</i>	<i>Postoperative</i>	<i>Pathological</i>
Acute Cholecystitis	6	5	1
Acute Cholecystitis with Stone	4	4	1
Chronic Cholecystitis	30	25	10
Chronic Cholecystitis with Stone	77	80	84
Choledocholithiasis	3	5	1
Lymphocytosis	0	0	19
Cholesterosis	0	0	6
Aucte and Chronic Cholecystitis with Probable Stone	1	0	0
Acute and Chronic Cholecystitis	0	1	0
Chronic Cholyecystitis with Hydrops	0	0	1
Chronic Cholecystitis with Abscess	0	0	1
Cyst of Gallbladder	0	1	0
Carcinoma of Gallbladder	0	0	1
Gangrenous Cholecystitis	0	1	1
Cholecystic Dyskinesia	0	1	..
Empyema of Gallbladder	0	3	0
Pain Right Upper Quadrant	1	..	..
Common Duct Obstruction	1	0	0
Postoperative Leakage	0	1	..
Chronic Appendicitis	1	1	2
Subacute Appendicitis	1	1	0
Renal Calculus	1	0	..
Cirrhosis of Liver	0	1	0

or 88 per cent of our cases. Fifty-three per cent of the Lahey group had cholecystectomy alone. Cholecystectomy with choledochostomy was performed in 11 or 10 per cent of the St. Joseph's group. Exploration of the common duct with cholecystectomy was performed in 41 per cent of the Lahey group. It is to be kept in mind that the patients seen in a large, regionally and nationally famous clinic would be expected to present more difficult and more complicated surgery because such patients would tend to gravitate to such a clinic. The higher incidence of exploration of the common duct in the latter group would be expected accordingly. Also the criteria for exploration of the common duct as employed by the Lahey Clinic and described by Adams and Stranahan are as follows: (1) frequent acute attacks of biliary colic, chills or fever, (2) past or present history of obstructive jaundice or laboratory signs thereof, (3) dilated or thickened common duct, (4) multiple small stones in the gallbladder, (5) unsatisfactory or suspicious findings on palpation, (6) sediment in aspirated bile from the common duct, (7) non-calculus gallbladder with biliary tract sym-

ptoms, (8) small contracted gallbladder, (9) acute or subacute pancreatitis or hepatitis. It will be seen by the reader that these criteria for choledochostomy cover a much broader spectrum than are generally employed and therefore would increase the percentage of common duct explorations in the Lahey Clinic group. In two of our cases cholecystostomy was performed comparing with 6 cases or 0.45 per cent in the Lahey series. Both of the cases in our group undergoing cholecystostomy were poor risk elderly patients. A partial cholecystectomy was performed in 1 case necessitated because of operative or technical difficulties. As incidental procedures, appendectomy was performed in 25 (21 per cent) of our series, biopsy of the liver in 1, ventral herniorrhaphy in 1, and anterior colporrhaphy in 1 case. Four hundred or 36 per cent of the Lahey group had incidental appendectomy.

ANESTHESIA

General anesthesia was employed in 102 cases or 84.3 per cent, spinal anesthesia in 3, spinal anesthesia plus pentothal in 6, local infiltration in 8, and general plus intercostal block

in 2. There are no comparable figures in the report of Adams and Stranahan.

CONCURRENT DISEASES

A number of different complicating diseases were encountered in this series, although there were very few cases in each type. One patient was a severe cardiac. One patient was admitted to the hospital with acute coronary thrombosis and developed an acute gangrenous cholecystitis while under treatment for this complaint. A cystocele was found in 1 case, an incisional hernia was present in 1, and one patient had diabetes mellitus which was under control upon admission. One patient had chronic hepatitis. An adenocarcinoma of the gallbladder was found in 1 patient upon examination of the excised specimen. Three cases or 0.3 per cent in the Lahey group were found to have adenocarcinoma of the gallbladder.

POSTOPERATIVE COMPLICATIONS

Ten patients of the 121 had some type of postoperative complications, mostly minor. There was 1 case each of superficial wound infection, thrombophlebitis of the left leg and urinary cystitis, pneumonitis with atelectasis and bundle branch block, paroxysmal auricular fibrillation, severe headache requiring neurological consultation, and 1 patient who had a postoperative external biliary fistula which was reoperated within 34 days of her initial operation. Although not strictly a complication 5 patients were discharged with T-Tubes in situ in the common duct. There was 1 fatality. The other complications of cholecystic disease such as pancreatitis, benign strictures of the bile duct, internal biliary fistulas and postcholecystectomy syndromes as described by Adams and Stranahan were not encountered in the present small series.

ANALYSIS OF DEATH

The one death in this series occurred in a 49 year old white female who was admitted to the hospital with a history of three months duration. She had been jaundiced on one occasion prior to admission and was jaundiced but with

out pain at the time of admission. Cholecystograms revealed a non-functioning gallbladder and an Upper G-I Series showed a dilated duodenum. On physical examination the patient was deeply jaundiced, presented a large liver and a mid-line mass which was not definitely identified preoperatively. The icterus index was markedly elevated in this patient. The preoperative medical diagnosis was carcinoma of the head of the pancreas or possible carcinoma of the gallbladder. The surgeon called in consultation made a diagnosis of common duct stone. The latter diagnosis was found to be correct upon operation in which a choledochostomy and cholecystectomy were performed. The patient had a very uneventful postoperative course until the fifth postoperative day when she suddenly went into shock, presented signs of marked hemoconcentration and in spite of very adequate and vigorous treatment expired. The medical opinion as to the cause of death was acute adrenal insufficiency. Necroscopy revealed marked ileus and changes in the adrenal gland consistent with the medical diagnosis of adrenal depletion.

SURGEONS AND OPERATIONS

This series of 121 cases were operated by a total of 27 different surgeons. The largest number of cases operated by any individual was 19. Seven surgeons performed 1 operation each.

CONCLUSIONS

No broad conclusions have been attempted in this review. However, all gallbladder surgery in a private hospital done by a number of different surgeons of different qualifications, background, and training, have been presented. A total of 121 patients underwent surgery. A total of 122 operations were performed with 1 death or a mortality of less than 1 per cent. It is the opinion of the author that the manner in which these patients were handled from the surgical point of view compares very favorably with the results obtained in a large nationally famous clinic group.



BASIC *Science* SEMINAR

PHYSIOLOGY OF SHOCK WITH SPECIAL REFERENCE TO ETIOLOGY AND THERAPY

Physiology of shock with special reference to Etiology and Therapy.
(excluding lower nephron nephrosis)

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Introduction:

Acute circulatory failure was first described by Le Dron in France, in 1745, as a clinical entity resulting from trauma and characterized by peripheral arterial spasm, capillary stagnation and general circulatory insufficiency. But, it was not until 1765 that the term "shock" began to appear in medical literature. It is generally accepted that James Lotta of Scotland was the first to use the term "shock."

The literature on shock is voluminous. Experimental physiology and clinical observations particularly on the traumatic shock during and since the first and second world wars have contributed considerably to put some light on this complex subject. This paper intends to summarize the literature with special emphasis to etiology, pathogenesis and therapy.

Definition of shock:

The term "shock," today, is practically applied to all types of acute peripheral circulatory failure, regardless of cause or multiplicity of causes. Just as there are many causes of fever, so there are many causes of shock. To use descriptive terms in association with the word shock, such as shock following hemorrhage, shock associated with peritonitis would probably clarify the complexity.

Various syndromes characterized by a sudden depression of cellular function not accompanied by circulatory insufficiency also are called shock. Insulin shock is a good example of this group. They will not be included in this paper. Shock caused by myocardial failure and pericardial tamponade will also be excluded from this discussion. The role of myocardium, however, will be discussed in pathogenesis of shock.

It has been customary to speak of a primary and a secondary shock. A distinction has been made by many writers between primary and secondary shock: though they are not in agree-

ment as to what contributes or causes the two forms. Most of them define primary (early) shock as an immediate or early response to trauma on a neuro-psychic basis; pain and emotional factors (such as great fear) playing an important role by causing reflex vaso-dilatation and decrease in relative blood volume, and a profound fall in blood pressure.

Recovery from the primary shock may be quite prompt, but if it prolongs it may develop into the secondary shock, which is the kind usually seen in the severely wounded or following serious or prolonged operations.

The acute peripheral circulatory failure which follows 3-4 hour or later after a severe tissue injury is called secondary shock or "delayed shock."

Pathological Physiology of Shock:

The appearance of a person in shock is characteristic. He lies quite still, apparently unconscious of his surroundings, but can answer questions slowly and correctly. The face is pale and gray, drawn and anxious, and the skin is cold, the temperature is subnormal, the pulse is feeble and rapid, the respiration is shallow.

Gregersen and Root have demonstrated that the signs which are shown by man in traumatic shock can be reproduced experimentally in dogs with the exception of sweating. In experimental shock in dog and clinical shock in man, thirst is present and ingested food particles are usually vomited.

In the experiments on the production of shock, it was found that shock could be produced by severe hemorrhage; repeated small hemorrhages; sufficient trauma to muscles; severe burns; crush injuries and by the application of a tourniquet.

When the chest of an animal in deep shock is opened the heart is found to be beating vigorously. The heart cavities are not completely

filled. The venous pressure is low, the cardiac output reduced. Marked reduction in the circulating blood volume is found. The systolic B.P. may be no more than 60 mm Hg.

Although early B.P. readings may be within normal ranges due to compensatory vasoconstriction in hemorrhagic shock, but in general, there is a fair correlation between the B.P. readings and the severity of blood loss.

Systolic B.P. Readings	Loss of % total blood vol.
→100 mm Hg.	15%
80-100 mm Hg.	25%
<60 mm Hg.	35-40%

B.P. in shock due to burns may be normal or elevated.

Slowing of the peripheral blood flow and reduction in the cardiac output occur early in shock and precede the fall in B.P. Therefore, it can be said that routine checking of the systolic B.P. is, in itself, of no value in determining the impending onset of shock, by the time patient's B.P. is lowered significantly, it being a late sign, shock is already present.

Haemoconcentration:

This is a significant feature of shock. Haemoconcentration is extreme in degree in burn shock and occurs as a result of plasma lost from the burned surface and the tissues surrounding the burn. In an intensive burn, 70% of the total plasma volume may be lost from the circulation within a few hours. The shock state following burn is attributed largely to the reduction in blood volume and to the increased corpuscular concentration of the blood.

As to the mechanism of haemoconcentration in delayed traumatic shock, it is not well known. The theory that the leakage of plasma from the capillaries could possibly occur as a result of an undue permeability of capillary wall has not been proved. The question whether long continued anoxia is causing increased permeability of capillaries anywhere in the body, has been subject to experiments. Fine and his co-workers, by tagging the plasma proteins with radioactive material so as to make their identity unquestionable, showed that the general capillary leakage does not occur. They favored another theory instead, namely the theory of pooling or "tapping" of the blood in the peripheral vascular bed so keeping large amounts of blood out of circulation. This theory has been given support by the findings of marked congestion of the

mesenteric vessels in shocked animals. Indeed, in post-mortem examination of a shocked animal or person, the liver and gastro-intestinal tract are intensely congested, the walls of the intestines are edematous and show petechial hemorrhages.

Erlanger gives further support to this conception by describing the packing of corpuscles in the dilated capillaries of the intestinal villi in shock. Mann found that, whereas about 24% of the blood volume of a normal animal is held in peripheral vascular areas and the remaining 76% in the heart and larger vessels, in shock 61% was trapped in the peripheral vessels. This 61% of whole blood volume is out of general circulation. So it is quite clear that any great enlargement of the capillary bed would alone reduce circulating blood volume effectively enough to cause marked reduction in the venous return and consequently cardiac output, thus causing a physiological vicious circle. After a critical point has been passed in diminishing cardiac output, lowered B.P. and reduced blood volume, progressive oligemic anoxia of the tissues leads metabolic changes and damage to certain vital organs such as liver, kidneys, heart and brain. The liver seems to play an important role in shock. Fine, Seligman and Frank recently reported a most interesting series of experiments in connection with the part played by liver. In dogs, they established an anastomosis between the aorta and portal vein by using a vessel graft and then these dogs were put in shock by bleeding them from the carotid artery until their systolic B.P. were stabilized around 50 mm. Hg. Under these circumstances, the pressure in the portal vein still remained higher than of control animals. Shock in these dogs with aorta-portal anastomosis appeared to be reversible—7 out of 8 dogs survived while 15 out of 17 control animals died of shock.

This protective effect of aorta-portal anastomosis is due to improved blood flow through the liver, consequently better oxygenation of the liver. According to the hypothesis, normally oxygenated liver detoxifies or inactivates the depressor principle which is found in the blood stream of shocked animals.

Kidneys are also affected seriously by anoxia which causes injuries to the renal cells resulting in the condition called the "lower nephron syndrome" which will not be included in this discussion.

As to the heart, Wiggers believes persistent low B.P. and anoxia damages myocardium and he has found that cardiac output is rarely restored fully after transfusion.

Opdyke and Foreman showed that during standardized hemorrhagic shock in dogs coronary flow decreased to 30-60% of control flow during the 50 and 30 mm. Hg. hypotension periods and flow resistance was greatly decreased. Vasodilatation appeared to play a prominent part in the decrease in resistance.

During shock important changes take place in the blood. The slowing of the blood flow is accompanied by a decrease in O_2 consumption and progressive decreases in pH and arterial CO_2 content and progressive increases in the concentration of lactate and phosphate; there are slight increases in pyruvate and sulfate, and the base bound by protein is reduced. Elevation of the Lactic and Pyruvic acids and the rise on the L/P ratio in hemorrhagic shock results from the predominance of anaerobic over aerobic carbohydrate metabolism, especially in muscles, in the presence of peripheral circulatory failure. In this situation, energy is derived from glycolysis where the end product is lactic acid.

A rapid return toward normal of blood Lactic and Pyruvic acids and L/P ratio follows transfusions.

Seligman, Frank and Fine also showed that the disappearance of injected glucose from the blood was poor during the hemorrhagic shock. This was the same with pyruvic acid. Following transfusions clearance of both substances was found to be normal.

Blood potassium has been subject to special studies with the purpose to find out if hyperpotassemia is responsible for cardiac death in shock. According to the recent investigation, potassium in blood seldom exceeds 8 mm per liter, a level at which they noted only minimum EKG changes. According to Winkler and Hoff, it is exceptional for death to be caused by cardiac arrest resulting from potassium auto-intoxication. It is believed that potassium may reach toxic levels in only final stages of shock.

No changes have been reported in blood Na. or Ca.

STAGES OF SHOCK

Davis has divided circulatory failure into five stages:

1. Primary (early shock):

Primary shock does not involve a reduction in

blood volume necessarily. It usually appears shortly after trauma, particularly if much pain is associated with it. The skin becomes cold, clammy and pale, sweat appear on the face and patient is in typical shock. Spontaneous recovery usually takes place quickly if responsible cause (pain or fear) is eliminated.

2. Impending secondary (delayed) shock:

$\frac{1}{2}$ to 12 hours after the primary insult impending secondary shock may occur. Patient may appear quiet, talkative or extremely restless. During this period the B. P. may be within normal limits or even elevated. The pulse may be 60 to 150 beats per minute. This is a transitory phase and the peripheral circulation is still in compensation.

3. Decompensated secondary (delayed) shock:

This is the decompensation phase of the shock and its significant physical sign is the low B.P. There is a fall in both systolic and diastolic pressure with a reduction in the pulse pressure. Pulse rate is increased to 100 to 200 beats per minute. The diastolic pressure may be so low that it cannot be determined. Arteriolar-capillary rate may be delayed to 15 seconds or more.

4. Pseudo irreversible shock:

This is midway between decompensated and irreversible shock. Appearance of the patient is like in the irreversible shock. But the difference is in the fact that the circulatory failure can still be corrected if sufficient amount of blood is given.

5. Irreversible shock:

By irreversible is meant the unfavorable response to transfusion which follows the 90 minutes period of hypotension in 50 mm Hg. systolic B.P. and 45 minutes in 30 mm Hg. systolic B.P. in experimental shock. Acidosis also develops during this hypotension period. There are certain definite signs which indicate irreversible stage of shock: continuous low B.P. in spite of apparently adequate transfusions, greatly increased pulse rate, Cheyne-Stokes breathing, severe mental depression, continuous cold clammy skin and cyanotic nail beds. All these indicate the final stage of shock prior to death.

ETIOLOGY OF SHOCK

Many theories have been advanced in attempts to explain the genesis of the shock state. These theories will be mentioned here briefly before further discussion of the subject.

1. Inhibition theory:

It was tried with this theory to explain shock

as a result of the predominance of the inhibitory side of organ and tissue function induced by injury.

2. The theory of vaso-motor paralysis:

According to this theory, following injury there is a marked reduction in vascular tone resulting from the stagnation of blood in the abdominal viscera.

3. The Exhaustion theory:

Is based upon exhaustion of the vaso-motor and other vital centers as a result of overaction of these centers following psychic, traumatic, toxic or thermal stimuli.

4. The "fat embolism" theory.

Stated that the main cause of the findings in shock were emboli of fat to the brain, lungs and other organs.

5. The theory of "adrenal hyperactivity" blamed hyperfunction of the glands for causing the onset of shock.

6. The "adrenal exhaustion" theory blamed adrenal failure.

7. The "acidosis theory" which believed that the blood pressure fell because of a lowered alkaline reserve.

8. The "acapnia theory" which with it was tried to explain the diminished venous return. According to this theory hyperpnea occurred first, then acapnia, then failure of the vaso-pressor mechanism, then tissue asphyxia.

9. The "vaso-constriction and capillary congestion" theory which stated that increased hydro-static pressure because of the stasis in the veins caused extravasation of serum into the tissues.

10. The theory of "traumatic toxemia":

The toxins produced by the injured tissues cause acute circulatory failure.

11. The theory of the "actual loss of red cells and plasma":

Acute circulatory failure is caused by losing blood into the injured tissues.

It is clear that some of these theories deal more with the mechanism of shock than with its cause. Theories dealing with etiology can be reduced to three:

1. Toxemia Theory

2. The theory of local fluid loss

3. Shock of nervous origin

1. *The Toxemia theory of shock:*

This theory was originally based on the hypothesis that the main features of shock were due to the action of a histamine-like depressor sub-

stance formed through the destruction of tissue, especially of muscle.

It has been known since 1919 that when injected into animals in doses of 1 mgm. per kilogram of body weight, histamine produces shock-like features via its depressor effect upon the circulation, namely, a fall in blood pressure due to peripheral vascular dilatation. Furthermore, in experimental anaphylactic shock in dogs it has been shown that during the period of sensitization following a foreign protein injection the histamine content of the liver of sensitized animals is increased. However, when these dogs are re-injected with the same foreign protein after an interval of 12 or 14 days and shock produced the histamine content of the liver is reduced below normal.

Bayliss and Cannons' experiments seemed to prove the toxemia theory of shock in which a histamine-like substance, or histamine itself, was the responsible agent. These observers crushed the limbs of animals and reported that a fall in B.P. did not result so long as the vessels of the injured part were occluded, though the nerve trunks remained intact. Upon restoring the circulation a fall in B.P. occurred. On the other hand when they cut the nerves, leaving the circulation a fall in B.P. occurred. On the shock could not be prevented.

Other experimental physiologists who have repeated Cannon and Bayliss' experiments have not been able to obtain the same results. Besides this, attempts have failed to isolate a toxic substance from traumatized tissues; and extracts of these tissues have been injected into normal animals with no production of shock, blood from shocked animals has been injected into the veins of normal animals without harm; one shocked animal has been transfused with blood from another shocked animal with benefit.

The question of a toxic factor in burn shock is confused for the reason that a distinction has not always been drawn between the stage of shock and the later stage of toxemia which results from the absorption of proteolytic products derived from the burned tissues or of bacterial origin. The question of a burn toxin, however, has been investigated. Robertson and Boyd reported that an alcoholic extract of burned skin but not of normal skin contained a toxic agent which caused death when injected into normal animals. The blood or red cells, but not the plasma, of burned animals also contained

the toxic agent. They came to the conclusion that a toxin formed in the burned tissues was absorbed into the blood stream and carried by the red cells. Vogt excised a burned area of skin from a guinea pig and transplanted to another, the first animal survived but the second died.

It is also known that the blood of burned patients contains a high concentration of histamine. However, no clear correlation in time between the Histamine concentration in the blood and the onset of shock has been found.

Shock producing exogenous toxins:

Extracts of *Ascaris Suum* (Ascaron): Intravenous injections of crude or purified of the round worm and hydatid cystic fluid cause a profound state of shock in dogs, cats, rabbits and guinea pigs which is undistinguishable from anaphylactic shock.

Mann and Essex demonstrated that in the dog the liver was chiefly responsible for the extreme hypotension since liverless dogs were not seriously affected by doses of ascaron that killed intact animals.

Thomas and Essex showed by making casts of the hepatic vasculature that the hepatic veins were thrown into such intense spasm that passage of blood from the liver was prevented. Although many drugs have been tried, none has been able to relieve the hepatic venous spasm caused by ascaron.

D.L. substance: This is a toxic substance discovered by Delezanne and Ledebt who found that cobra venom mixed and incubated with egg yolk produced a toxic substance that killed guinea pigs and rabbits. In this kind of shock, severe constriction of pulmonary vessels has been found.

2. The theory of local fluid loss:

This theory intends to explain traumatic shock entirely on the basis of the escape of blood or of plasma from the vessels at the site of the trauma.

Blalock showed that after bruising a limb by beating it with a hammer, the quantity of fluid which accumulates within the part, as estimated by comparing its weight with that of the sound limb, is sufficient to cause the fall in B.P. Some experiments revealed that as much as a third or a half of the total blood volume was calculated to have entered the traumatized area.

It is true that in many instances the quantity

of circulating blood lost locally is sufficient to reduce the blood volume to the fatal level, but in other instances the fluid locally lost is not sufficient in amount to cause death. When death occurs with a fluid loss than which would prove fatal if lost by external hemorrhage, then another factor must be looked for.

Nathanson, Pope, etc. developed a technique allowing the collection of fluid from a muscle after ischemia was produced by the application of a tourniquet for some hours. They found that the muscle gained Na. and lost K. There was a loss of fluid into the leg locally from the body. The exudate which collected produced shock in one animal in four following injections.

3. Shock of nervous origin:

Since the failure of isolating a toxic substance to cause shock and the failure in some cases to explain the shock on the basis of local fluid loss, the role of the nervous system in shock has been investigated.

It is known that the sensory nerve impulses play a great part in production of primary shock. Whereas the role played by nervous system in secondary shock is rather complicated.

Experiments to determine the part played by the nervous system in shock fall into two classes: A. The first consists in the attempt to produce shock by stimulation either traumatic or electrical, of different levels of the nervous system, central, peripheral as well as sympathetic system. And it was found that the only way to produce, by nerve stimulation, anything like shock, was by stimulation of the cardio-aortic or carotid sinus nerve over a period of from 6 to 8 hours. But this is something that is obviously not seen in ordinary trauma.

B. Second way of investigating the role of nervous system in shock is to avoid afferent impulses and see if this would effect the development of shock.

Wang of Columbia University has found that "animals survive muscle trauma with greater degree of blood reduction if the afferent impulses from the injured limb are interrupted by previous deafferentation.

O'Shaughnessy and Slome also found that blocking the nerve pathways by spinal anesthesia delayed or prevented the onset of shock in animals whose limbs had been traumatized.

As closing this chapter of discussion on the etiology of shock, it seems reasonable to make a statement that, while the theory of toxemia

remains wide open to further investigation, nervous impulses play an important role in production of secondary shock though blood loss into the injured tissues plays a part.

TREATMENT OF SHOCK

Success in treatment depends upon early recognition of shock. Failure is because of "two little or too late" treatment.

It was tried to emphasize in a previous chapter of the paper that the routine checking of the systolic B.P. is, in itself, of no value in determining the impending onset of shock. The principal early signs of impending shock are an increase in pulse and respiratory rate, a deterioration in the color of the mucosa, a deterioration in the arteriolar-capillary rate and a softening of the pulse.

There are a few tests may help us in early recognition of shock. These will be mentioned here briefly.

The Tilting Test:

This test is based on the fact that upright position, in the presence of a reduction of blood volume, produces a stress on the circulatory system. Increase in pulse rate with a slight fall in systolic B.P. and moderate increase in the diastolic pressure occurs when the patient is brought from the supine to the semi-upright position.

The Tourniquet Test

The basis for this test is that in the presence of a decreased blood volume an artificial temporary reduction of the circulating blood volume by means of a tourniquet will result in a fall of the arterial B.P. The B.P. cuffs are applied to the upper parts of the thighs and the cuffs are inflated to a pressure just above the diastolic B.P. level. In a normal person changes in B.P. do not occur, but in a patient suffering from shock a fall in the arterial B.P. will occur.

Circulation Time

It has been found experimentally on dogs by Painter and Overman that changes in circulation time as determined by the fluorescein method within the first two hours following the traumatic procedure, is a simple yet sensitive early sign in the pattern of slowly developing shock. According to the authors, in many cases a true prognosis can be made on the basis of two consecutive determinations of the circulation time. In general it can be said that animals with impending shock in which the circulation time shows a gradual prolongation will die, whereas animals that survive show a slow im-

provement in the circulation time. It is generally accepted that a circulation time of over 30" by the fluorescein method indicates a grave prognosis. Two determinations of circulation time separated by an interval of one hour or longer should be done. And it would seem wise for practical purpose, to institute preventive therapy whenever the circulation time is found to be above the normal range.

Principles of Treatment

The main purpose of treatment in shock should be removal of causative factors (such as pain and fear in primary shock, stopping of bleeding in secondary shock) and restoration of normal physiology of circulatory system.

As physiologic basis for successful treatment of clinical shock two things are essential:

1. To restore the failing circulation
2. To restore the failing (anoxia) tissues.

The circulation can be restored, in most instances, by replacing the deficit in blood volume. A method of estimating whole blood volume in shock is of considerable value not only as an index of the circulating deficit, but also as a measure of the volume required in replacement therapy. This brings up an important question in treatment of shock. It should be remembered that while inadequate replacement of deficit in circulatory volume leads to failure in treatment and consequently puts patient in irreversible shock whereas over-replacement of circulatory deficit results in cardiac failure.

The usual method of blood volume determination in experimental shock is to determine plasma volume, by injecting Evan's blue dye into the circulation. After plasma volume determination by the diluting of the dye in the plasma, the total blood volume is estimated by using the following formula:

$$\text{Total blood volume} = \frac{\text{plasma volume} \times 100}{100 - (0.96 \times \text{hematocrit})}$$

0.96 is hematocrit correction factor.

As to the question how and with what should the deficit in the blood volume be replaced, it must be remembered that the purpose of replacement is not only to correct the reduction in blood volume and cardiac output, but to supply sufficient amount of oxygen to the tissues and by doing so to correct main pathology, namely oligemic anoxia. For this, it is obvious that the circulating blood must contain adequate amount of hemoglobin. Therefore, in hemorrhagic and traumatic shock where whole

blood loss is involved replacement should be made with whole blood, whereas in burn shock where circulatory deficit is mainly due to plasma loss, plasma should be given.

For practical purposes, saline infusion can be used for temporary replacement until blood or plasma is obtainable. Saline produces a much smaller and more transitory increase in blood volume. The temperature of the saline infusion is important: warm infusion stimulates the sino-auricular node and quickens the heart rate while a cold infusion has the opposite effect. A hypertonic saline infusion also exerts an intra vascular osmotic action, attracting water into the vessels from the tissue spaces.

Urinary output gives us a fairly good idea of prognosis and success of therapy. 20-50 cc. output per hour is a good sign.

The following table demonstrates hemodynamic response and increase in oxygen transport following treatment with albumin, blood and isotonic saline solution. 22 cases of shock shown in this table are all traumatic except 3 cases of burn shock which were treated in Bellevue Hospital.

This investigation indicates that the concentrated human albumin is an effective agent in the treatment of acute traumatic shock in man. The albumin injected into the circulation is largely retained, providing no further bleeding or exudation of plasma occurs. It is still remaining in the circulation at the end of 6 hours.

The albumin retained holds in the blood stream amounts of fluid approximately comparable to its osmotic activity. Thus, in the cases of Cournand, Noble and Breed, 1 gm. albumin retained resulted in an average increase of plasma volume of 23 cc. This fluid may have drawn into the blood from the tissues, or may have been simply retained, if additional cry-

stalloid solution was also administered. No unfavorable side effects have been noted from the use of this preparation. The increase in plasma volume produced by the injection of albumin effects a marked improvement in the circulation. Specifically, all the primary changes associated with recovery from acute shock are observed: increases in right auricular pressure (venous return) in arterial pressure, and in cardiac output. Clinically, the patients are improved.

Comparison of the effects of albumin with those of rapid saline infusion have shown that saline produces a much smaller and more transitory increase in blood volume and the increase in cardiac output with saline infusion, while considerable, is not sustained.

In comparing the effects of albumin (or plasma) with those of whole blood: by giving albumin, the arterial oxygen transport is restored to normal only if the cardiac output is correspondingly increased above normal. Cournand's table shows this. But it should be remembered that there is a limit in the capacity of the heart to produce further compensatory output if hemorrhage continues. Eventually, the heart and circulation can no longer compensate and cardio-vascular failure will occur. In cases recovering from shock, this danger will be greater in the presence of any additional strain, such as operation, or if infection develops.

Gelatinoid products in treatment of shock:

Gelatin solutions are being used as substitute for plasma in replacement of circulatory deficit. These solutions are prepared from beef-bone collagen which is subjected to dialysis and clarification to free the solutions from pyrogenic substances. Purified gelatin solutions jell at low temperature. Shortly before administration, the solution should be brought to a fluid state by

Comparison of Average hemodynamic response and increase in O₂ transport following treatment with albumin, blood, isotonic solution from Noble, Breed, etc.

Type of Therapy	No. of Cases	Time of Measurement	Average Total blood volume cc per sq. M	% Average hematocrit	Average Auricular pressure MM H ₂ O	Average Cardiac output litre per min. per sq. M.	Average O ₂ Consumption cc per minute per sq. M.	Arterial O ₂ transport plus	Amount of Material injected and retained
Albumin 25 gm in 100cc	6	initial final differential	1863 cc 2207 plus 344	36 26	0 plus 27	2.27 4.15 plus 1.88	154 189 plus 35	298 425 plus 127	injected 66 gm retained 42 gm added crypt. 852 cc
Blood	10	initial final differential	1734 cc 2261 plus 527	31 33	plus 10 plus 41 plus 31	1.76 2.88 plus 1.12	137 161 plus 24	201 356 plus 155	infused 809 cc retained 88% added crypt. 921 cc
Saline	6	initial final differential	2070 2234 plus 164	37 32	plus 37 plus 57 plus 20	2.81 3.94 plus 1.13	154 170 plus 16	379 487 plus 108	infused 1644

warming to 37 c. Intra-venous administration of gelatinoid solutions have been shown to be effective in preventing the development of shock in traumatized dogs. In clinical shock, gelatinoid preparations have been found to produce a satisfactory colloidal osmotic effect as plasma. Approximately 80% of gelatin is excreted in urine within 48 hours. There is some doubt if gelatin is utilized by the body. But, no significant changes have been found in blood urea and amino acid levels.

Intra-arterial transfusion:

Among the reasons for giving blood by artery instead of by vein are the following:

1. Blood pressure is restored to normal levels within a few minutes and the pressure is controllable.
2. Blood volume deficits are automatically corrected. That amount of blood will be taken into the circulation which is required to fill it at a given arterial pressure.
3. When the heart and respiration have failed, blood given into an artery often brings about resuscitation.

It has been observed by Page of Cleveland clinic that when blood was transfused by artery, little more than half the amount of blood was required to restore arterial pressure than when blood was given by vein.

Page took serial x-ray photographs of a dog deeply in shock while it was receiving an arterial transfusion of radio-opaque material. They showed that the kidneys filled first, and immediately thereafter the coronary circulation.

The apparatus consisting merely of a pressure reservoir with a manometer connected to the femoral or radial artery. If the need is urgent, an 18 gauge needle may be inserted, pointing toward the heart, or a glass cannula may be tied if time permits. Heparin solution is used to prevent coagulation in the cannula and tubing, but blood itself in the reservoir may be citrated unless very large amounts are to be given, when the use of heparin becomes more desirable. Care also must be taken to avoid air emboli.

According to Page, intra-arterial transfusion with this apparatus is a simple procedure. If the blood pressure is 30 mm Hg. or less, the

pressure in the reservoir should be set 20 mm. higher, and blood allowed to flow in. The pressure is then raised 20 mm. gradually each time, until the systemic pressure is 100 mm. Hg. At this pressure, the patient's artery should be left open to the reservoir for a while to make it sure that the pressure will hold.

Arterial transfusions have greater value in thoracic surgery. The mortality rate from injuries of the mediastinal vessels is high. Though the hemorrhage may be surgically controlled, death may result from loss of blood and shock. In this case, intra-aortic transfusions have proved to be of considerable value in combating shock. Oxygenated blood is more effective if given by intraaortic method, thus, reducing anoxemia as well as replacing circulatory blood volume.

Supplementary treatment to transfusions:

Levine and his co-workers have emphasized the need to consider hemorrhagic shock treatment from an anti-acidotic point of view. In their animals, following 2-3 hours of serial bleeding and its consequent decline of B.P., a severe acidosis developed which remained uncorrected after the returns of all withdrawn blood. Of their animals, 75% entered the irreversible shock state and died. When acidosis was corrected by supplemented administration of alkalinizing agents along with the reinfusions of withdrawn blood, the transition from impending to irreversible shock during the post-reinfusion period was, in many cases, permanently arrested.

Acidosis develops during the hypotension period. The transition from impending to irreversible shock occurs during the 90 minute hypotension period rather than in the post-reinfusion period. It seems worthy, therefore, to determine whether, by preventing acidosis from developing during the hypotension period, it might not be possible to prevent the transition from impending to irreversible shock during the period of hypotension.

Wiggers and Ingraham have published the results of their experiments with alkalinizing agents in treatment of hemorrhagic shock in dogs.

The table on the following page shows the results.

Series	Recov.	died	% mort.
Control (untreated)	3	10	77%
Na Bicarbonate or Na lactate supplemented to re-infusion of withdrawn blood	3	10	77%
Continuous NA Lactate infusion during hypotension period	1	5	83%
Continuous Na Bicarbonate during hypotension period	7	6	47%

In this experiment Na Lactate given 0.87 gm. per kilogram and Na Bicarbonate 0.65 gm. per kilogram of body weight of dogs. Only minimum amount of water used to dissolve the alkalies.

The above table shows that while supplementation of alkalinizing agents to retransfusion did not change the mortality rate in irreversible stage of shock in comparison with those of controls, continuous NA Bicarbonate infusion during the hypotension period reduced the mortality rate to 47%. In contrast to this beneficial action of Na Bicarbonate, administration of Na Lactate did not reduce the mortality rate at all in their experiments. The authors are convinced that Na Lactate is neither effective anti-acidotic agent nor useful in the treatment of severe hemorrhagic-hypotensive conditions which may progress to irreversible shock if not combated. The hypothesis is that the anoxia of hemorrhage may decrease the ability of the liver to metabolize lactic and amino acids, attributing this failure to a substance present in tissues which becomes active under anorobic conditions.

Following table shows effect of alkalinizing agents to the plasma CO₂ volume of shocked dogs.

Series	No. of Dogs	volume		
		cont.	90" hypo-	post-
Na Lactate fatalities	5	48.3	28.3	32.3
Na Bicarbonate fatalities	4	45.8	40.6	38.8
Na Bicarbonate recoveries	6	44.0	55.3	51.7

Value of Ascorbic acid in supplementation of transfusions

As it is known, Vitamin C is reported to raise the natural resistance of guinea pigs, monkeys and man, and its requirements are greatly increased during infection, in wound healing and

probably under all conditions of stress. Its use in the treatment of traumatic injuries as well as in post-operative shock has been strongly advocated. In the laboratory, the survival time of the cats, bled to 50% of their original blood volume, has been prolonged by the I.V. administration of 1 gm. ascorbic acid. De Pasqualini's following table shows his experiments with Vitamin C:

	No. of animals	died of shock	survived
Treated with Vitamin C	18	1	17
Controls	17	15	2

De Pasqualini administered ascorbic acid in considerably large doses of 200 mgm. intraperitoneally 15 minutes prior to bleeding except 5 animals which received 100 mgm. intra-arterially via carotid artery 5 minutes previous to bleeding. The controls were treated in the same way, the vitamins being replaced by physiologic saline.

Unger greatly reduced the mortality rate from traumatic shock in guinea pigs, rats and mice, the minimal effective dose 100 mgm. per kilo. According to Unger the effect was not due to vitamin C since the oxidized preparations gave the same results.

Up to this part of discussion, replacement of blood volume deficit and supplementation to replacement therapy was discussed. Combating anoxia is an important part of the therapy in shock. The O₂ tent is useful in two ways, by reducing respiratory efforts and giving ready access to oxygen to the red cells. Efforts have been made experimentally to transport O₂ in the plasma, but without any success so far as combating anoxia is concerned. The other way of increasing the O₂ carrying capacity of the blood is by restoring the blood volume with fluids. Restoration of volume alone, even though it dilutes the red cell concentration, by increasing blood pressure accelerates the red cell flow and thus increases their efficiency. But it is obvious that if great reduction in red cells has taken place, O₂ inhalation and mere replacement of circulatory deficit would not be of a great value unless deficit in red cells replaced. In this case transfusion of oxygenated whole blood should be the treatment of choice.

Morphine in treatment of shock:

Morphine has been widely used in shock. Attention has been called against using morphine in shock.

Gregersen showed that the I.V. injection of 2 mgm. Morphine Sulfate caused, in normal dogs, a sharp drop in the respiratory rate and volume, in O_2 consumption, and in B.P. and heart rate. It is interesting to note that although the cardiac output was depressed, the calculated total peripheral resistance increased. When the same dose of morphine was given to animals in hemorrhagic shock, there was a temporary increase in the O_2 , arterial CO_2 and cardiac output. But these evidences of improvement in the circulation did not alter the eventual outcome or prolong the survival time. In dogs in severe traumatic shock, Gregersen found that the morphine only exaggerated the circulatory disturbances.

Gregersen calls attention to the fact that even small doses of morphine may have a considerable effect on a failing circulation.

Conclusion:

In this paper it has been attempted to summarize the literature on physiological pathology of acute circulatory failure. Pathogenesis and etiology, mainly toxemia and local fluid loss theories and nervous factoris in development of shock; and physiological basis of therapy including restoration of circulation and measures to combat anoxia were discussed.

As concluding my words, I would like to express my appreciation to Drs. Frederick Lese-mann and Louis Hirsch, and Miss Mabel Lucey,

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PHOENIX *Clinical* CLUB

MASSACHUSETTS GENERAL HOSPITAL CASE NO. 29421

The Case History in this discussion is selected from the Case Records of the Massachusetts General Hospital, and reprinted from the *New England Journal of Medicine*. The discussant under Differential Diagnosis is a member of the staff of the Massachusetts General Hospital. The other discussants are members of the Phoenix Clinical Club.

A forty-one-year-old night watchman was admitted to the hospital because of intermittent gas pains of ten years' duration.

The patient was apparently well until about ten years prior to entry, when he developed intermittent attacks of indigestion in which he

suffered from epigastric gas pains and the sensation that his stomach was "tied up in knots." The pain occurred approximately half an hour after eating, or when he had gone three or more hours without eating, and lasted for about an hour. It was relieved by anything that would "break the gas" and produce gaseous eructations such as soda, milk or food. The attacks were sometimes precipitated by cabbage, pork and fried foods. Vomiting of undigested food, especially fried foods, sometimes gave relief. The vomitus was never bloody, nor did it contain coffee-grounds material. The last attack of vomiting occurred six weeks before admission. Three years before admission, following x-ray examination at a community hospital, he was

placed on a strict ulcer regime, with prompt symptomatic relief as well as gain in weight. The diet, however was discontinued six months later and the symptoms recurred. Nine months prior to entry, while working in a dusty atmosphere, he had two or three attacks of vomiting and his symptoms increased in severity for two months, at which time he obtained another job, with some relief in his condition. In the three or four months before entry he experienced daily distress after almost every meal. There was anorexia and a weight loss of 15 pounds. He subsisted mainly on soups, milk and cream, crackers, tea and so forth. He became progressively weaker.

He had been constipated most of his life and had habitually taken various laxatives. There had been no back pain, heartburn, dizziness or fainting. He smoked one package of cigarettes daily and drank some beer and a little whisky. He had experienced considerable financial difficulties.

Physical examination showed a well-developed small, wiry, tense man with evidence of recent weight loss. There was no pallor. He was endentulous. The tongue was reddened and coated with coarse papillae. The heart and lungs were normal. The abdomen was scaphoid and soft. There was no tenderness, spasm or palpable masses. Peristalsis was active. Rectal examination revealed a small, firm, non-tender prostate. Considerable tenderness was elicited superiorly and on the left, where a questionable soft mass was palpated.

The blood pressure was 125 systolic, 80 diastolic. The temperature was 98.6°F., the pulse 76, and the respirations 20.

The blood showed a red-cell count of 4,300,000, with a hemoglobin of 14 gm. The white-cell count was 6800, with 63 per cent neutrophils. The urine was normal. The stools were guaiac negative on eight occasions but gave a 4+ test on one occasion. The blood Hinton test was negative. The nonprotein nitrogen was 20 mg. per 100 cc. The blood protein was 5.6 gm. per 100 c.c., the carbon dioxide combining power 21 millimols per liter, the chloride 95.9 milliequiv. per liter and the blood sugar 74 mg. per 100 cc. Gastric analysis showed no free acid before and half an hour after histamine injection; the values for total acidity were 5 and 18 units respectively. Both aspirations gave a ++ guaiac test.

X-ray examination showed a normal esophagus. Just below the cardia there was an ulcer crater measuring 1 by 1 cm., with a rigid, soft-tissue mass surrounding it. This filling defect measured 4 cm. in length. The remainder of the stomach and duodenum was normal.

The patient was placed on a gastric diet with tincture of belladonna, 15 drops, and phenobarbital 2 gr., three times a day. His condition improved. Gastroscopic examination eight days after entry showed a normal antrum and pylorus and an increased reddening of the body of the stomach in the upper part, with a few streaks of bright-red blood. There was a marked verrucous, cobble-stone appearance in the upper 4 or 5 cm. near the cardia; no ulcer crater could be demonstrated. Following gastroscopy, the epigastric symptoms recurred but were relieved by Creamalin 45 cc. every two hours. A gastric analysis on the fifteenth day showed 25 units of free acid and a total acid of 35 units half an hour after histamine injection. X-ray examination after one month on the medical regime showed the ulcer crater to be smaller than it was formerly, but the crater was surrounded by what appeared to be a polypoid mass extending along the lesser curvature for about 8 cm. The lesser curvature was rigid in this area.

An abdominal exploration was performed six days later.

H. L. FRANKLIN, M.D.

After mulling over this case for a considerable time, and perusing a treatise titled "Disease of the Digestive System," and a few other pertinent pieces of literature bearing upon the same subject, I have come to the conclusion that the correct diagnosis is so obvious that I am going to play a one-shot and if I am wrong, or very wrong, I am going to resign from this club and go fishing. I shall, therefore, say right off that our patient was suffering from that broad and general inclusive term known as dyspepsia. Although we have good evidence that there is pathology in the stomach and perhaps in sufficient quantity to account for all of the symptoms, it is perhaps pertinent to say that without the benefit of x-ray and gastroscopy we might be somewhat in the dark as to whether it originated in the stomach or outside. One author states that for every six cases of dyspepsia five have their origin outside of the stomach. To name a few; tuberculosis, heart disease, anemia, nephritis, cirrhosis of the liver, neuroses, dis-

ease of other parts of the intestinal tract. We have, however, positive evidence of some stomach pathology three years prior to admission, though his stomach trouble had existed for seven years prior to that. At this time, after an X-ray examination, he was placed on an ulcer diet and improved. I presume some evidence of ulcer was found at that time. Bloomfield states that if we can rule out duodenal ulcer, which I think we have done, then the three most common diseases of the stomach are gastritis, both acute and chronic, gastric ulcer, and carcinoma. The incidence about as follows: gastric ulcer 9, carcinoma 7, gastritis 45. There is considerable evidence that gastric ulcer was present, indeed this diagnosis was made three years before entry and a short while before operation, both by x-ray and clinical symptoms, and I think this diagnosis would have stood had they not later, upon a gastroscopic examination been unable to find an ulcer, but instead found an increased reddening of the upper part of the stomach with a few streaks of bright red blood, with a verrucous cobble-stone appearance in the upper part of the cardia. One month after this report and after an ulcer regime an x-ray report shows an ulcer crater, but smaller than the previous examination, and surrounded by what appeared to be a polypoid mass extending along the lesser curvature for 8 cm., and the stomach wall in this area was rigid. This is somewhat confusing since all x-ray reports show a crater, and the gastroscopic does not find it. We shall have to hear the surgeon's or pathologist's report to settle this point. Templeton and Schindler in a study of 44 cases of ulcer found that only 33 were demonstrated with both methods. Four were seen with the scope and not the x-ray, and seven were seen with the x-ray and not through the scope. Perhaps it is this discrepancy that caused this case to be presented.

From an evaluation of the symptoms and findings and on a basis of statistical chances, I am going to assume that the diagnosis is between chronic gastritis, and gastric ulcer, perhaps associated with the gastritis, and cancer.

Syphilis is presumably ruled out by the negative Hinton, and tuberculosis, while it cannot be ruled out, to consider it would be far-fetched. I am assuming that by the record there is no evidence of t.b. elsewhere in the body and the G.I. tract otherwise is normal. The mention of a possible tender mass high up on the left side

upon rectal examination is probably a herring of some sort

Schindler states that in chronic gastritis there is an infiltration and proliferation of the gastric mucosa leading to a thickening. It comprises about 41% of all cases of chronic gastritis. The etiology is unknown. It cannot be recognized grossly in the postmortem specimen except in cases of tumor-simulating proliferation of the mucosa. Microscopically three different forms may be distinguished, although grossly at gastroscopic examination the same picture is observed with all of them, namely; 1. hypertrophic interstitial gastritis, 2. hypertrophic proliferative gastritis, 3. hypertrophic glandular gastritis.

1. In hypertrophic interstitial gastritis may be seen dense lymphocytic infiltration between the long body glands, usually together with enlarged lymph follicles which have no sharp limits.

2. In hypertrophic proliferative gastritis the lymphitic structures of the glands are unaltered, but on top of them there is a grotesque proliferation of the surface epithelium which grows to form irregular large nodes, which double the thickness of the mucosa.

3. In hypertrophic glandular gastritis inflammatory processes are relatively few, but there is a tremendous over-growth of the glandular apparatus, which may treble the thickness of the mucosa.

In (2) and (3) tumor formation simulating carcinoma may be observed. The gross appearance is best studied with the gastroscope. In healthy adults the mucosa is glistening and smooth, while in patients with hypertrophic gastritis it has a dull, velvety, loose, spongelike appearance. The area involved later becomes nodular with a typical "cobble-stone" surface. The changes are found most frequently in the body, although sometimes they may be seen in the antrum. Inflammatory, small and large mucosal hemorrhages are frequent. From time to time small grey or yellow ulcerations develop. The symptoms are chiefly gastric. Severe ulcer-like pains are present, sometimes they may not be relieved by administration of milk or alkali. The patient states that he has always had a weak stomach, has had to be careful about his food, and vomiting rarely occurs, profuse hemorrhages occur and may even have a fatal outcome. The physical examination and tests give essentially

negative results, although occult blood may be found in the stools.

This description is consistent with the gastroscopic description in our case and in a like manner the symptoms of indigestion over a period of ten years are consistent with a chronic gastritis.

There is no way that I know to say that we are not dealing with a cancer superimposed on an old gastritis or ulcer. The weight of evidence is that perhaps cancer is a little more likely to develop in an area of gastritis or ulceration than in a healthy stomach, certainly if it is cancer, it is a late comer. The reference to the gastric analyses furnishes no evidence one way or the other, due to the variation in the ability of individuals to secrete acid and the extent of the lesion and its location.

However, some free acid was recovered after the last histamine test. This might be considered a point against cancer. He had lost some weight, there was a mild anemia, all of which could have been due to poor diet, rather than cancer. It is worth mentioning, I believe, that although this patient had had stomach distress of all sorts for a period of ten years, and was under observation for three years with a probable diagnosis of gastric ulcer, he was treated medically. It was only after the polypoid mass was discovered that an exploratory operation was performed, certainly they suspected that a cancer had developed in that area.

I am just as unable to make a correct diagnosis in this case as it was to the eminent medical men at the bedside and in the laboratories. I think they were thinking of gastric ulcer with a cancer superimposed, or chronic hypertrophic gastritis. The x-ray shows an ulcer, the gastroscopist does not find an ulcer but what seems to be a chronic gastritis.

I am going to guess that he did have a chronic hypertrophic gastritis with nodular or polyp formation, perhaps a healed or active ulcer. Now, I hope that what I have written here is not too fuzzy. Here's to more and better fishing until we meet, again, probably.

Read before the Phoenix Clinical Club, May 14, 1951.

DIFFERENTIAL DIAGNOSIS

Dr. William B. Breed. It seems to me that there are two possibilities to be considered. Either this lesion was a benign one throughout its course or it started as a peptic ulcer, then degenerated and became malignant. The history certainly is suggestive of the latter supposition.

You will note that the early story is indicative of peptic ulcer with periodic pyloric obstruction and relief of symptoms on an ulcer regime, as well as recurrence of symptoms when the regime was discontinued.

The dusty atmosphere of his new job can be disregarded. I have no thoughts about that.

Two or three months prior to entry he began to have continual discomfort directly after eating, with anorexia and loss of weight but no typical symptoms of ulcer. Up to that point this could well have been a benign ulcer near the cardia that had degenerated and had become malignant. Gastroscopy possibly confirmed the nature of the process: the upper part of the stomach wall was verrucous and cobblestone in appearance.

Dr. Edward B. Benedict: That does not mean malignant disease. That means gastritis.

Dr. Breed: I am glad you are here, Dr. Benedict. The record states, "a marked verrucous, cobblestone appearance." There was no mass. Will you describe it as you remember it?

Dr. Benedict: A verrucous and cobblestone appearance may mean chronic hypertrophic gastritis.

Dr. Breed: In a localized area?

Dr. Benedict: Sometimes localized, sometimes generalized. This was fairly well localized.

Dr. Breed: You introduce the idea here at once that this lesion was benign. Let us go ahead and see whether we can put that together with the second examination by x-ray, which described a polypoid mass extending along the lesser curvature, which a rigid musoca.

In passing, I should say that one has to consider lymphoma of the stomach in any condition like this. However, I am willing to conclude that if this was a polypoid mass it probably was not due to lymphoma. Do you ever see polyps in lymphoma, Dr. Benedict?

Dr. Benedict: Not discrete polyps.

Dr. Breed: You saw no polypoid mass?

Dr. Benedict: No, but I could not see the ulcer. It was in a part of the stomach that is difficult to visualize.

Dr. Breed: No polyp was seen on the first x-ray examination. We might see both sets of film.

Dr. Milford Schulz: Here are the films made at the time of admission, and there is no gain saying the fact that there is an ulcer with what appears to be a mass of soft tissue about it.

In addition you can see an irregular soft-tissue mass extending into the cardia.

Dr. Breed: What does that mean to you? Is this soft-tissue infiltration?

Dr. Schulz: By all the rules it should be a carcinoma.

Here are the films made after a month of treatment. The ulcer is somewhat smaller. You still see all this thickened verrucous soft tissue extending into the air-filled and barium-filled portion of the stomach. It is true that there are quite prominent mucosal folds throughout the stomach; in a recent similar case, however, in which a diagnosis of cancer was made, the condition at operation proved to be gastritis and not carcinoma.

Dr. Breed: This is not that case by any chance

Dr. Schulz: No.

Dr. Breed: Kindly show me the polyp.

Dr. Schulz: There is no true polyp, but there are numerous soft-tissue masses extending into the gas bubble of the stomach and displacing the barium. Here is the defect in the stomach in which the ulcer lay. By all the rules that should be a neoplasm.

Dr. Breed: I am going to stick to the rules, because it is a fairly straightforward history and I see no reason for trying to be too smart. The patient had an ulcer for ten years and then developed a cancer at the side of the ulcer.

Dr. Benjamin Castleman: Is there any other comment?

Dr. J. H. Means: I think it could be a leiomyoma. I am not offering that as one of the possibilities, but it seems to me that I recall that they are apt to run a more or less benign course for some years and then become increasingly malignant.

Dr. Castleman: They usually give a long history of bleeding and become larger extremely slowly. A few of them do become malignant, however.

Dr. Means: What about other tumors of the stomach, such as fibroma?

Dr. Castleman: I do not believe that an accurate differential diagnosis of the various intramural tumors—fibroma, neurofibroma and leiomyoma—can be made clinically or by x-ray, or even microscopically in some cases.

Dr. Means: I discussed that point with Dr. George W. Holmes, some years ago. He claimed that when they were smooth and round it was

one thing, and when lobulated it was another. How about the significance of these differences? Does the lobulation mean anything?

Dr. Castleman: A definite lobulation is perhaps more in favor of a neurofibroma, but all these tumors tend to be well circumscribed and round. They often have a central ulceration

Dr. Schulz: An intramural tumor is usually quite characteristic in appearance roentgenologically. It displaces or smooths out the mucosa rather than showing soft-tissue masses extending into the lumen of the stomach.

Dr. Breed: I shall have to add that he had gastritis as well as cancer.

Dr. Benedict: I think the ten-year history is in favor of a benign lesion.

Dr. Breed: Such as?

Dr. Benedict: Benign ulcer. Of course that brings up the question, Do benign ulcers ever become malignant? A lot of people think that they never do.

Dr. Castleman: I was about to take issue with Dr. Breed's statement.

Dr. Breed: I have two against me.

Dr. Castleman: We are certain that an ulcer remains an ulcer and does not degenerate into a carcinoma. I believe that there are a few cases with definite ulceration in the stomach, proved roentgenologically, that ten years later develop carcinoma in the same location—that is, in the ulcer. If one checks some of these histories of long-standing ulcer with carcinomatous degeneration one often discovers that the ulcer was in the duodenum and not in the stomach, and things of that sort. It is true that carcinoma can remain in the precancerous state,—carcinoma in situ,—limited to the mucosa, without invasion over a long period of time. We have seen several examples of this condition*. Furthermore, precancerous lesions have been known to exist for six or seven years in the cervix. These carcinomas in situ may ulcerate; they are, however, ulcerating carcinomas, rather than carcinomas developing in benign ulcers.

Dr. Breed: Along that line, it did occur to me when I was studying this case that the patient might have had a duodenal ulcer and that this was a new malignant lesion. I am willing to go back to that idea. Since the pathologist

*Mallory, T. B. Carcinoma in situ of stomach and its bearing on histogenesis of malignant ulcers. *Arch. Path.* 30:348-362, 1940.

insists that ulcers do not degenerate, I shall probably have to agree; but I still think that the lesion was malignant.

Dr. Means: The picture could fit with carcinoma in situ, could it not?

Dr. Castleman: It could, although ten years is a long time for carcinoma in situ; most of them are under five years in duration.

Dr. Ronald C. Sniffen: This area of the stomach is rather unusual for carcinoma in situ, is it not?

Dr. Castleman: Yes; most of the lesions have been in the prepyloric region.

Dr. Breed: The patient may have had a duodenal ulcer for ten years and then developed cancer of the stomach in the cardia. I am willing to accept that.

CLINICAL DIAGNOSIS

Carcinoma of stomach.

DR. BREED'S DIAGNOSIS

Carcinoma of stomach.

Duodenal ulcer?

Chronic gastritis.

ANATOMICAL DIAGNOSIS

Acute and chronic phlegmonous gastritis, with gastric erosions and ulcerations.

PATHOLOGICAL DISCUSSION

Dr. Castleman: The surgeon's operative notes state that he was able to feel two ulcers, one close to the cardia and one 5 or 6 cm. below

that. He thought that the lesion was probably benign, but since he was not absolutely sure, and since the ulcers were high in the cardia, he believed that the patient would do better by having a resection.

When the stomach was opened, we found innumerable ulcers. Some were old, measuring 2 or 3 mm. in diameter, with a greenish-fibrinoid base, the result of necrosis. Between the ulcers the mucosa was markedly edematous and red and the rugae were prominent. This appearance reminded me of that of ulcerative colitis, with bridges between the ulcers. It might be called a phlegmonous gastritis.

Microscopic sections showed an acute and chronic inflammatory reaction throughout the whole wall, with necrosis of the mucosa and the formation of erosions and deep ulcers. We were unable to find a chronic ulcer that the patient might have had for ten years. It may have been in the duodenum, or more recent disease may have covered it.

Dr. Benedict: Were they true peptic ulcers, or erosions?

Dr. Castleman: Both were present.

Dr. Benedict: How do you distinguish between them?

Dr. Castleman: One speaks of an erosion if the destruction extends to the muscularis mucosa; if it goes beyond that, it is an ulcer. The etiology is the same.

There was no evidence of malignant disease.

NEWS ITEMS

RECENT MEDICAL GRADUATES SELECTIVE SERVICE

It has come to the attention of the National Advisory Committee that some individuals who may be in either Priority I, II, III or IV, and who obtained their professional degree this June have failed to register as required under Public Law 779. If they are under 26 years of age they are, of course, regular registrants, but should also register as special registrants. It is imperative that these individuals register at once. (Of course, if they are in the active Reserve it is not necessary for them to register.)

1952 FELLOWSHIP DUES DISCONTINUED

The Board of Trustees of the American Medical Association at a meeting held in headquarters recently, decided there would be no Fellowship dues for 1952. The dues, the Board felt, are no longer required since A.M.A. members are now paying membership dues and, furthermore, the Fellowship dues requirements were too confusing to members as a whole.

Fellowship dues of \$5.00 for 1951 are still payable.

THE *Secretary's* MESSAGE

THE ARIZONA MEDICAL ASSOCIATION, INC.

Many times the question has been asked: "Of what advantage or benefit is membership in the Arizona (State) Medical Association?"

This article is dedicated in an endeavor to answer this oft-repeated query.

First, what is or what comprises the State Medical Association? In case some of you do not know, your State Association is a constituent body of the American Medical Association. In this capacity it acts as an intermediary between the national organization level and the local component County Medical Societies in carrying out the policies and purposes of the parent organization. As you know, each component County Medical Society operates under charter and at the pleasure of the State Association, and therefore it is essential that there be a very close and cooperative relationship between these two levels in order that the activities of each may be ever closely coordinated.

The pattern of organizational structure in your State Association parallels that of AMA, comprising a House of Delegates, consisting of representation from among the membership of the County Medical Societies, acting as the official governing body. It elects the Officers and Council, which group functions as the administrative and financial operational medium. This body in turn appoints membership to its Professional and Public Relations Boards, in addition to seven standing committees, namely: History & Obituaries, Industrial Relations, Legislation, Medical Defense, Medical Economics, Publishing, and Scientific Assembly. As occasion arises special committees are also appointed, presently including Civilian Defense, Constitution & By-Laws, Grievance, and Procurement & Assignment. This latter group (P&A), in addition to dental and veterinarian groups, also serves as the Arizona Advisory Committee to the (National) Selective Service System. We will not go into detail as to the scope of operation of each of these boards and Committees. Suffice to say that their activities, as indicative of their respective titles, are varied and extensive within their individual fields. It would be amiss, however, not to mention here and pay tribute to those members, officials of your organization, who give so unstintingly of their time and energy without remuneration or personal aggrandizement in the interest of the medical profession. They are the workers and to them should go our everlasting appreciation and gratitude.

It is obvious that within so large a national organization reaching into every corner of the land, it is confronted almost daily with problems, both professional and administrative, requiring the most deliberate study and solution. Your State Association works in close harmony with AMA in its efforts to cope with such problems as your local representative and spokesman. Likewise, on the state level, it institutes procedures and initiates actions of direct local concern. Medical defense against suits of alleged malpractice and matters legislative consume considerable time and preparation, to safeguard your interests, which alone would adequately merit continuing membership in and active support of your State Medical Association. Medical Economics, Industrial, Professional and Public Relations each are chapters deserving of recognition within themselves and require constant vigilance and attendance by their respective boards and/or committees. Possibly no other public relations project is contributing so much toward improved physician-Patient relations than the operations of your state and local (Maricopa and Pima) Grievance Committees. This is being accomplished through your cooperation and participation in investigations. Scientific Assembly may not be widely understood, but this Committee is responsible for the presentation of your Annual Meeting. This activity in itself is becoming big business and demands constant attention and planning between meetings. Technical exhibits and scientific sessions require much thought and able supervision. The outstanding scientific program presentations and continuing success of this meeting reflects the effort put forth by this group.

Your State Association is representative of the medical profession. Its organization—your organization—is ever alert and ready to serve. It is deserving of your confidence and support.

Editorial

ARIZONA MEDICINE

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The Editor sincerely solicits contributions of scientific articles for publication in ARIZONA MEDICINE. All such contributions are greatly appreciated. All will be given equal consideration.

Certain general rules must be followed, however, and the Editor therefore respectfully submits the following suggestions to authors and contributors:

1. Follow the general rules of good English, especially with regard to construction, diction, spelling, and punctuation.
2. Be guided by the general rules of medical writing as followed by the JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. (See MEDICAL WRITING by Morris Fishbein.)
3. Be brief, even while being thorough and complete. Avoid unnecessary words. Try to limit the article to 1500 words.
4. Read and re-read the manuscript several times to correct it, especially for spelling and punctuation.
5. Submit manuscript typewritten and double-spaced.
6. Articles for publication should have been read before a controversial body, e.g., a hospital staff meeting, or a county medical society meeting.

The Editor is always ready, willing, and happy to help in any way possible.

PREPARATION OF THE AGED PERSON FOR SURGICAL OPERATION

It has been thought for a long time that the principles of surgery are altered by the age of the patient. Thus we have text books on Pediatric Surgery and there are numerous articles on the surgery of the aged. Nevertheless, the primary surgical principles are similar or identical in various age groups although the

application of these principles to the problems which specific patients presents may require modification because of the factor of age. It is not always possible to draw a sharp line and state that every patient past sixty is aged, for many patients past this age are in reality in a better state of health from the standpoint of the aging process than are patients in the latter forties or fifties.

The processes of aging are not uniformly progressive in all people, nor are the criteria of the aging process now so clearly defined that they are readily established in their entirety. It has been stated repeatedly that we are as old as our cardiovascular systems, but the problem is not nearly so simple as that. The cardiovascular system is not the only one affected by the aging process.

Partial impairment of the functional capacity of certain viscera may occur at any period of life, due to preexisting systemic disease or perhaps excessive or protracted intake of alcohol, excessive smoking or even persistent overeating. It may result from prolonged exposure to certain noxious agents, as in industry, or from accumulated fatigue or any one of the many other sources of injury.

It is, therefore, impossible to generalize on the problems which the patient past middle age presents from the surgical view, for the conditions which have surrounded the individual during life and the diseases to which he may have been subjected vary greatly in extent. With older patients, individualization is far more essential than with younger adults or children. There are, however, certain physiological changes which the processes of aging are known to bring about more or less uniformly in all individuals. These, without a doubt, create some additional hazards to surgical procedures and should therefore lead to certain modifications in surgical practice. While the surgical principles may remain the same, expediency requires their modification, in one direction or another, in order that the morbidity and mortality of operations upon the elderly be reduced to a minimum.

The surprising thing is that every surgeon who has been interested in the surgery of the

aged has come to recognize that, properly protected, the risk to the senile patient is not nearly as great as it is commonly believed, even for extensive operations. Realization that the special hazards are not insurmountable has led to gradual extension of the radical surgery in certain diseases to those who previously were denied possible benefit. In order that this be further extended, it is important that certain physiological facts be more widely understood.

It is generally believed that the aging process is accompanied by a decrease in the volume of the circulating blood. It would seem improbable for the plasma volume to remain constant when, as a result of the changes of senescence the blood vessels become less elastic. Wiggers and other investigators have repeatedly called attention to the fact that the distensibility of our blood vessels diminishes with age. In addition to the sclerotic and atheromatous lesions so common in senescents, other more subtle changes occur.

The inability of the vessels of the aged to adjust rapidly to changing conditions of blood volume creates one of the major hazards of prolonged anesthesia and extensive operation, especially if the latter is associated with considerable trauma. There are now a number of factors which must be considered.

The very marked and nearly instantaneous manner in which vasodilatation and vasoconstriction can occur in normal individuals provides an effective protective mechanism of paramount importance where rapid changes in the size of the vascular bed are necessary. Large amounts of sodium chloride solution, plasma, serum or blood may be injected into an individual with a normal cardiovascular system without the slight danger. In the aged, however, very much smaller amounts may produce cardiovascular incompetency because the vascular system is no longer easily distensible. In a similar manner the loss of even a considerable amount of the blood or plasma volume may be well tolerated by an individual with normal vascular response and a normal heart, because of rapid vasoconstriction and the simultaneous increase in the heart rate lead to maintenance of a normal minute cardiac output. In such circumstances vasoconstriction provides an important protective mechanism against cardiovascular incompetency. On the other hand, where the myocardium is not so strong and vasoconstriction not so easily

accomplished, a much smaller loss of circulating blood volume may be attended by the most serious of consequences.

In the preparation of an aged individual for surgical operation, a survey of the cardiovascular system is, of course, in order. Except for Stokes-Adams attacks, and the discomfort produced by abnormal cardiac rhythms, the heart symptoms that an aging person complains of are the manifestations of heart failure. Dyspnea produced by exertion considered inadequately by the patient, or breathlessness prolonged beyond the ordinary recovery period should be suspected as of cardiac origin, as should any type of chest or arm discomfort having a repeated relationship to exertion or emotion. In general it may be said that there is no way to determine abnormal cardiovascular aging beyond the discovery of a history of angina pectoris, or its painless equivalents, except by finding definite cardiac enlargement, persistent hypertension, calcific aortic stenosis, a loud constant apical systolic murmur, clearly abnormal cardiac rhythms, signs of congestive failure, or typical electrocardiographic patterns of conduction defects or myocardial ischemia. Frequently physicians ask: "Will this patient's heart withstand an operation?" This indicates a belief widely held that anesthesia and operation impose upon the heart burdens that must be seriously considered in deciding for or against an operation upon the patient with heart disease. The basis upon which this belief rests is that during operations there may be observed disorder of the heart's rhythm, rapid heart action, thready pulse, low blood pressure, cyanosis and disturbances of respiration. It is true that most of these are circulatory manifestations, but they do not indicate incompetency of the heart. As Marvin of Yale pointed out many years ago, for the purpose of anesthesia and operation, the heart that is damaged but is carrying on an adequate circulation under normal conditions at life is equivalent to the normal heart. In other words no matter what the heart size may be, no matter what thrills or murmurs may be present over the precordium, no matter how far or in what directions these murmurs may be transmitted, if the patient has been leading a life involving moderate activity without symptoms the heart may be regarded as equivalent to a normal one and it may be safely assumed that it will behave properly during anesthesia

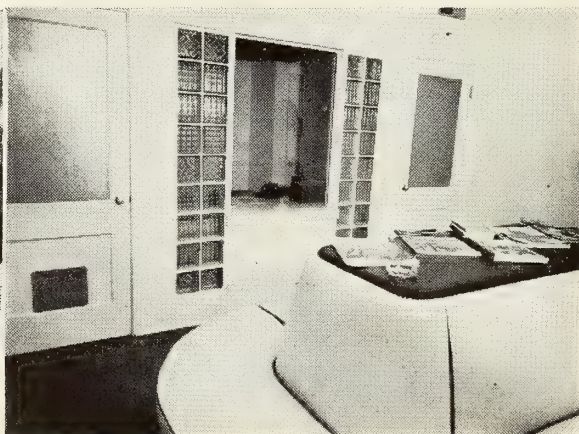
and operation. There are certain exceptions, however, that must be mentioned. Syphilitic heart disease with aortic insufficiency, complete heart block, coronary artery disease including bundle branch block offers certain hazards as patients with these conditions may suddenly die.

Many of these aged individuals who are suffering from malnutrition and chronic debility and osteoporosis and nitrogen balance is disturbed. Testosterone and estradiol aid in the addition of protein to the tissues of the body. They promote the formation of new protoplasm. Obviously a hormone cannot substitute for adequate supplies of food including a proper share of proteins, but there is evidence that the sex steroids strongly influence the manner in which foods will be utilized. It was shown by Albright that nitrogen balance was improved by administering testosterone to a patient who had been receiving inadequate proteins; the further destruction of the patient's own tissues, as a source of fuel, was "inhibited." In chronic debilitated states such as rheumatoid arthritis, "tissue anabolism was reinitiated" by androgen. In the practical application of this medication, one takes advantage of the fact that androgens and estrogens act as synergists in protein synthesis, but antagonize each other's actions on the reproductive tract and sexual

characteristics when a suitable ratio of dosage is administered. The ratio may vary from 20:1 to 50:1. The two hormones are administered in a single injection of about 1 cc. and are given 2 or 3 times weekly. For example in the ratio of 20:1 testosterone is given 0.8 cc. of the 25 mg./cc. combined with estradiol benzoate 0.3 cc of the 3.33 mg./cc. dosage. The ratio may be changed depending upon the patient's response. In the preoperative treatment of patients with osteoporosis, these sex hormones are of definite value, since it is now recognized that osteoporosis is primarily a disease of the protein matrix of the bone. The soft-tissue in which calcium is laid down deteriorates then the calcium is released. It has been shown that testosterone or estradiol, or the two given in combination, will reverse the protein losses and permit recalcification to take place. In summary then it can be said that the aged person should be prepared carefully for surgery and the complete evaluation of the cardiovascular system should be carried out and congestive failure should be remedied. If there is any evidence of prostatic obstruction, this should be relieved. Chronic debilitated conditions the patient and those suffering from malnutrition as well as osteoporosis should be treated with the sex gland.



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TOPICS OF *Current Medical* INTEREST

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By GUILLERMO OSLER, M.D.

This 'Osler' business can become even more complicated. . . . A Baltimore friend of ours has written as follows,—"I am glad to know that another Osler has appeared. You may recall that William Osler's nom de plume was Egerton Y. Davis. Last year one of the House Staff at Hopkins sent a fabulous account to a scientific journal of an occurrence he had seen while on a cruise the preceding summer. (It concerned the love-making of a couple of whales). The journal took it seriously, published it, and sent the check for the manuscript to the author, 'Egerton Y. Davis, Jr.' The check was dropped in the hospital corridor **perhaps** by accident; it was turned in to the superintendent; and the gag soon was recognized. . . . The whole hospital has been chuckling, because the story can't be revealed—and no one dares to claim the check!"

Surgeons and anaesthetists (and a few ordinary people too) will be interested in the report by Kay and Blalock of Johns Hopkins on a new help in cases with CARDIAC ARREST. They report that intracardiac calcium chloride has been effective when epinephrine failed. Two to 4 cc. of a 10% solution was injected.

ONCE UPON A TIME someone gave the Comstock Hospital in Tucson (Crippled and Tuberculous Children) the complete setup for a dental room. . . . TIME HAS PASSED, and do you know what? No dentist has been available to do the job. Not even from the dental association, it is said. . . . SUDDEN THOUGHT—maybe someone will see this sad little note, and put a bug in a dentist's ear. They can't all be so busy that one or two couldn't man the chair for a couple of hours every week or so.

PATIENTS WITH GOITER AND HYPERTHYROIDISM do not bother Arizona physicians very often. The state is not in a goiter belt. . . . It should be remembered, however, that the 'Great Lakes area' is not the only source of goiters, and that several states bordering Arizona are goitrogenic. Utah and Nevada of the Mountain area and California of the West Coast area are involved.

Two 'cause and effect' items were published separately (and with a straight face) by the ARIZONA PUBLIC HEALTH NEWS. . . . Item No. 1—The x-ray technician who has recently been in charge of the traveling unit has just been married to a former technician. They have moved to Oklahoma. . . . Item No. 2—The future schedule for the x-ray bus has been cancelled. It will be

started again as soon as a technician can be found.

Wyeth Inc. reports that a major use of streptomycin is in domestic fowl. About 75 per cent of the chickens and turkeys on the market have had the drug, due to its effect on sinusitis, etc. . . . As a result, the total sale of SM almost equals that of penicillin, and streptomycin is often in short supply. Wyeth makes a preparation much used by veterinarians.

The status of such costless journals as 'Modern Medicine' never seems very clear, altho they abstract excellent articles, quickly, and are often the source of entertainment and education. Perhaps we can't be much impressed by something for nothing. . . . Now, however, we have a reason abruptly to take a surprised look. . . . Dr. A. E. Hedback, who has been the fine editor of Modern Medicine, is retiring after 20 years. The new editor, believe it or not, is DR. WALTER C. ALVAREZ! . . . For years thousands of physicians have envied the versatility and imagination of Dr. Alvarez. No one, but no one, has exceeded his industry. Now, when he becomes the head of a project, it promises to be interesting. It also sets the project up a bit further.

Wolff of Washington, D. C. has recently surveyed the death toll from RHEUMATIC FEVER in childhood thruout the United States. . . . One of the oddities is the low mortality rate in ARIZONA, while that of Utah is constantly above the average. This latter variant is especially notable in boys from 15 to 19 years, and it is unexplained. . . . The differences in contiguous states "merit a more thorough examination".

The Bulletin of the N.T.A. describes NEW TB DRUGS in the news. (The abbreviation 'TB' is now official). . . . 'Vinactin A' is an antibiotic, made by Ciba, effective in mice. . . . 'G-469' is a French product, similar to TB-1, also effective in mice. . . . The Lebanese have used a sulphur-containing compound, combined with vitamin C. . . . The Parke, Davis 'Viomycin' is an antibiotic, previously reported, and still struggling for recognition. . . . None of these drugs has been safely useful in humans up to the present date.

NEWS DEP'T.—The appointment of Dr. E. B. Jolley to the STATE BOARD OF HEALTH seems like a wise and interesting choice. It brings an industrial physician (Phelps Dodge Corp.) to a position where he can be of special help. He is a World War II veteran, and has good connections with national medical groups.

The advancement of Dr. W. Randolph Lovelace of nearby Albuquerque to chairmanship of the ARMED FORCES MEDICAL POLICY COUNCIL seems like a good move. Dr. Lovelace, once of the Mayo Clinic, has been head of the section of surgery of the Lovelace Foundation—a 'little Mayo Clinic' in New Mexico. He has had rare training, and has done some fine basic work in aviation medicine. As memory serves, he is the 'L' in the BLB oxygen mask, and he was a co-winner of the Collier Trophy Award in 1940.

'Hospital Topics' is a buyer's guide for hospitals. The October issue had a picture of CLYDE W. FOX on its cover. Dr. Fox is the administrator of the Washoe Medical Center at Reno, but was the catalytic agent while the Tucson Medical Center was in its most active evolution. He not only helped build, but he obtained approval by the American College of Surgeons. . . . We can bet five to one that, when the Washoe problem is solved, he will be off to another job with a challenge.

The granddaddy of all chest surgeons (as well as several other types of cutters) was DR. F. SAUERBRUCH of Berlin, who died in July at the age of 76 years. . . . Dr. Sauerbruch developed thoracoplasty, the low and high pressure chambers for lung resection, surgery of the heart, restorative operations on the war-disabled, etc. He was a great teacher and writer.

WATER NOTE OF THE MONTH.—Can you hold out until 1985? Hold out without more water, that is? . . . President Conant of Harvard told the American Chemical Society that we may expect to have plenty of fresh water from the ocean, due to cheap and abundant power, about 1985. . . . Thirty-four years to wait—unless Mr. Lewis Douglas and Co. can get it sooner from the clouds. . . . I'd like to bet a peso with Mr. Conant that someone does the trick closer to 10 than to 35 years.

ANTIBIOTIC MILESTONES.—OZENA (atrophic rhinitis) may be controlled to varying extents by instillations of streptomycin solution (plus vasodilators,) and occasionally plus penicillin, bacitracin, and gantrisin. . . . The legion of 'cures' for TRICHOMONAS VAGINALIS VAGINITIS is augmented by aureomycin. It has been used locally in powder or gelatin form with success. Relapses occur, especially in pregnant women. Terramycin is now being tried in suppository form. . . . A new report re-emphasizes the value of penicillin as a protection from respiratory infection in cases of ASTHMA. A delayed action drug was used, in doses of 1,200,000 units every 3 or 4 days. Claimed success, 70% control. . . . Massive therapy for ENDOCARDITIS caused by a resistant organism really means BIG these days. A case is reported where an average daily dose of 86 million, repeat, 86 million, units was given for 28 days, with recovery. Intravenous route is preferable to avoid tissue damage. (Remember the days when 40,000 units per dose was the new 'massive' therapy?) . . .

Terramycin is now highly favored for that disease of Indians, Arabs, and wrestlers—TRACHOMA. It is miraculous for early and acute disease, only moderately less so for chronic lesions. Local therapy is preferred to systemic, ointment to solutions.

Keep an eye on the new method of determining GASTRIC ACIDITY. Segal, et Al., have eliminated the gastric-tube by using an ingested resin which has an attached substance for ion exchange. A quinine indicator is used. . . . If free HCl is present in the stomach, the quinine will be replaced by hydrogen ions; the quinine is liberated, absorbed from the intestine, and excreted in the urine; a test for quinine in the urine then shows the gastric situations. . . . Some such test should be very useful.

LOCAL TALENT.—We constantly hope for medical research and papers from Arizonans. Most papers arise from a series of cases; most series arise from specialization. . . . A series which is mildly surprising, and which might make a neat report, is the 40 cases of alcoholism treated with Antabuse at the hands of Jackman Pyre of Tucson. . . . (In case someone else has more cases, maybe this note will smoke him out). . . . We are specially interested, not as an old alcoholic, but because Antabuse has been mentioned several times in this column since it was first described in the American non-medical press in 1949-50. Its first use by Jacobsen and Hald, in Denmark, began as recently as 1947.

Odds and Ends about GASTRO-INTESTINAL X-RAYING. Both ends, actually. . . . L. Ruzicks and Rigler of Minneapolis have described a double contrast method of VISUALIZING THE STOMACH WALLS. Barium is swallowed as usual; a stomach tube is passed; the barium is massaged so that it intimately covers the walls; the patient is placed in a supine position; 500 to 1,500 cc. of air is injected thru the tube; spot films are taken at intervals to show mural detail (before and during the escape of air and barium to the duodenum and esophagus) . . . 2. Levene and Veale of Boston believe that the ordinary barium enema routine is not satisfactory. They spray a THIN MIST OF BARIUM-WATER SUSPENSION onto the walls of the rectum, and sigmoid, and avoid the distention of other methods. (American Journal of Digestive Diseases).

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IN THE SUPREME COURT OF THE STATE OF ARIZONA

FRANCIS M. FINDLAY, M.D.,)
WILLIAM F. ORLANDO, M.D.,)
BRODA O. BARNES, M.D. and)
WALTER BRAZIE, M.D.,)

Appellants,)

—vs—)

THE BOARD OF SUPERVISORS)
OF THE COUNTY OF MOHAVE,)
STATE OF ARIZONA, and W. H.)
RIDENOUR, A. J. MULLEN and)
LEE STEPHENS, constituting)
the members of said Board,)
and A. E. WALLACE, Clerk)
of said Board, and JOSEPH)
A. COPPA, Manager, Mohave)
General Hospital,)

Appellees.)

No. 5328

Appeal from Superior Court of Mohave County

Honorable H. L. Russell, Judge

Judgment Reversed

Charles P. Elmer, of Kingman

Favour & Quail, of Prescott,

Attorneys for Appellants

T. J. Byrne, of Prescott, of

Counsel

Carl D. Hammond, of Kingman,

Morgan & Locklear, of Phoenix,

Attorneys for Appellees

STANFORD, Justice:

This is an appeal from an order of the superior court quashing a writ of certiorari and dissolving the stay that had theretofore been ordered at the time the writ was issued. There was also made an order dismissing the petition upon which the writ had been granted.

The appellants (petitioners below) are four of the five practicing physicians in Mohave County. Located at Kingman, the county seat, is a county hospital known as the Mohave General Hospital, authorized, directed, and maintained under the provisions of Chapter 17, Arts. III and IV, ACA 1939, relating to the powers of the board of supervisors in maintaining favorable health conditions. Incidentally, this was the only hospital in the county and

widely used by the residents of the northwesterly corner of the state. As a county hospital, it was completely under the control of the board of supervisors of Mohave County, who had provided a general manager therefor. On February 18, 1949, the respondent members of the board of supervisors passed a certain resolution or rule pertaining to the use of the facilities of the hospital by *any* doctor. This resolution, known as Resolution 111, is as follows:

"RESOLVED, That if any doctor using Mohave General Hospital facilities is requested by another doctor, using such facilities, to assist him professionally and that doctor refuses or fails to give such assistance, then such doctor shall not be allowed to use said hospital facilities thereafter, except only for his patients in the hospital at that time."

On February 26, 1949, petitioner Barnes was notified by respondent Coppa, manager of the hospital, that he would no longer be allowed the use of the hospital, with the exception of the patients which he was then treating in the hospital. He was later notified that authority for this action had been obtained from the respondent board and was the result of an alleged violation of Resolution 111, *supra*.

In August of 1949, the three remaining petitioners received similar notifications and were also prohibited from further use of the hospital facilities. No charges were preferred and no hearing was given petitioners prior to the notifications. A statement was added at the bottom of each notice that petitioners could request a hearing if they so desired.

On August 31, 1949, petitioners filed their petition for writ of certiorari in the superior court of Mohave County, the Honorable J. W. Faulkner presiding. It was thereupon ordered that the writ issue and the respondents were commanded to certify and return the complete transcript of the record and proceedings held regarding the above mentioned notifications which petitioners had received. All proceedings, subsequent to the issue of the writ were heard and determined by the Honorable H. L. Russell.

There was also incorporated in the writ a stay requiring the parties in the meantime to desist from further proceedings in the matter to be reviewed. The purpose of the writ was to secure a review of the actions of the board of supervisors. The petition for the writ alleged:

(1) that the board had exceeded its jurisdiction in finding the respondents guilty of violating the resolution without notice and without trial; (2) that the board had exceeded its jurisdiction in denying the use of the hospital facilities to respondents; and (3) that the board had exceeded its jurisdiction in the adoption of the resolution for the reason that the resolution was unconstitutional and void in that it was unjust, unreasonable and exceeded the discretionary powers of the board.

After the writ was issued, respondents filed their motion to quash, which was thereupon denied by the court. They then filed their response to the petition which contained a partial record of the proceedings before the board and also denied certain material contained in the petition for certiorari, further alleging that petitioners had requested no hearing after the notification of violation of Resolution 111 and termination of their use of hospital facilities. For further response, respondents also set out details concerning the alleged violation which were not contained in the record of proceedings of the board. In this regard, we note particularly that the only matter contained in the certified record, pertaining to the alleged violations, is a copy of the minutes of the said board, which states merely that Resolution 111 had been violated, no particulars being set forth. It is stated in the return that there was no transcript made of such proceedings.

The court, after taking the matter under advisement, issued its order dismissing the petition for writ of certiorari, quashing the writ theretofore issued and granting respondents their costs, which order was supported by the court's written findings of fact and conclusions of law, filed in pursuance of petitioners' request.

In the lower court, and here, respondents questioned the use of the writ of certiorari to challenge the constitutionality of the resolution. Their position in this behalf was, and is, that the writ of certiorari may not be used to review the actions of inferior tribunals, boards or officers in the exercise of legislative, executive or ministerial functions. We have heretofore ruled that the writ is confined to a review of judicial action, and then only to determine whether the inferior tribunal, board or officer has exceeded its jurisdiction or acted without jurisdiction. *Faulkner v. Board of Supervisors*, 17 Ariz. 139, 149 P. 382. In *State ex rel Andrews v. Superior*

Court, 39 Ariz. 242, 5 P. 2d 192, it was held that certiorari issues only to test jurisdiction and not to determine whether it was erroneously exercised. The inferior court must have jurisdiction of the subject matter, person and power to render the particular judgment which was given in order that the judgment be proof against attack by certiorari. *Wall v. Superior Court of Yavapai County*, 53 Ariz. 344, 89 P. 2d 624. In numerous other cases we have held that certiorari raises only the question of jurisdiction and not the erraneous exercise thereof. If the resolution in question is so unreasonable and so unjust as to be unconstitutional, then the board, in attempting to enforce it *was* without jurisdiction. The rights of these petitioners were materially and substantially affected by it as were the rights of their patients and of the residents of Mohave County that had necessity for the use of the hospital's facilities and who might be admitted as paying patients. The principle of law laid down in the case of *Mill v. Brown*, 31 Utah 473, 88 P. 609, is fittingly applicable in the instant case. The court in that case said:

"* * * If the law be unconstitutional, then the acts of the respondent which affect the rights of the applicant have no support, and are, therefore, void and of no force or effect. This inquiry goes directly to the power—jurisdiction—of respondent to act, not to his qualification to do so, and hence can be inquired into in this proceeding. We cannot assent to the doctrine that a citizen affected by a law may not, at any time and in any judicial proceeding, attack that law as being unconstitutional and therefore void. An unconstitutional law by which it is sought to affect the rights of the citizen is of no force or effect and would not bind any one. *Norton v. Shelby County*, 118 U.S. 425-442, 6 Sup. Ct. 1121, 30 L. Ed. 178. Any act, therefore, of the respondent affecting the applicant's rights, if such act is based upon an unconstitutional law, is both without and beyond jurisdiction, and therefore void. The first objection cannot be sustained."

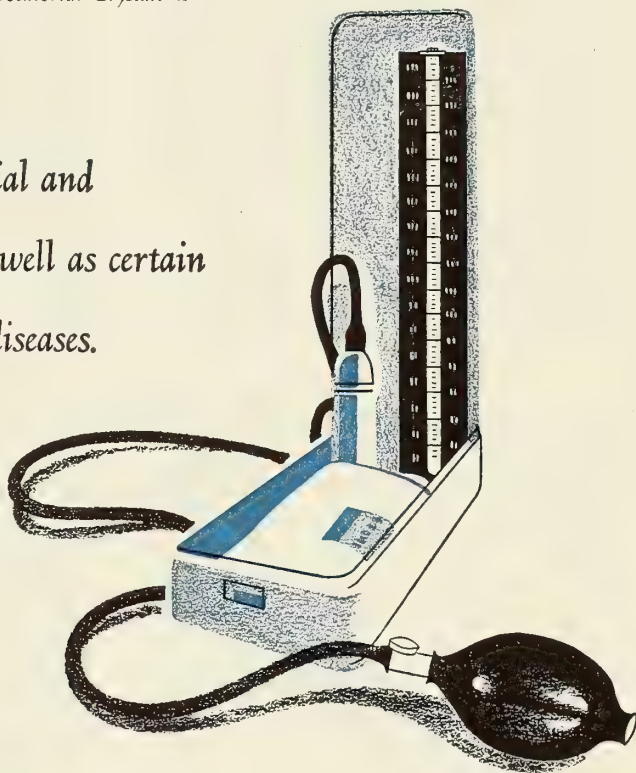
The board, in defending their actions, are relying upon their powers as conferred by law, pointing out that by the provisions of section 17-309, A.C.A. 1939;

"The board of supervisors, under such

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limitations and restrictions as are prescribed by law, may:

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"5. Provide for the care and maintenance of the indigent, sick and the dependent poor of the county; erect and maintain homes and hospitals therefor; provide in their discretion a farm in connection with the county hospital, and make regulations for working the same;

* * *

"17. Adopt provisions for the preservation of the health of their respective counties as necessary, and provide for the expenses thereof;

* * *

"22. Do and perform all other acts and things necessary to the full discharge of the duties as the legislative authority of the county government; but a supervisor shall not vote upon any measure in which he, or any member of his family, or partner, may be pecuniarily interested;

"23. Make and enforce all local, police, sanitary and other regulations not in conflict with general laws;

* * *

They also direct attention to section 17-404, A.C.A. 1939, which in part provides that:

"Except in emergency cases when immediate hospitalization or medical care is necessary for the preservation of life or limb no person shall be provided hospital or medical care hereunder without first filing with the board of supervisors * * * (indigent oath) * * *. The board of supervisors may admit into such hospital for hospital care, medical or surgical attention, any person other than an indigent who will pay, in part or in whole, for such hospital care, medical or surgical attention, under rules and regulations prescribed by the board. The admission of a paying patient shall not be to the inconvenience of any indigent patient."

In considering the reasonableness of the resolution under consideration we have taken into consideration the Code sections above referred to and that portion of section 17-349, A.C.A. 1939, wherein it is expressly provided that

"* * * Any person other than an indigent

who has been admitted to the county hospital, may employ, without expense to the county, a physician or nurse who shall be permitted the necessary use of the hospital facilities or equipment. * * *"

It is thus seen that a paying patient has a right to employ his own physician. Does this regulation impinge upon this privilege? If the rule is enforced the patient is restricted in whom he may employ, for the regulation provides that he may not employ a doctor who has not acceded to the regulation and agreed to assist any other doctor professionally, presumably in the hospital. In other words, the doctor, before he may prescribe for his patient, must first agree that he will aid and assist any other doctor in the hospital; under what terms and conditions we do not know. Presumably, he might be required to assist without any assurance of being compensated for his services. He might be required to assist in an operation which in his honest judgment is unnecessary or should be deferred. Undoubtedly, any person worthy of the title of "Physician" or "Doctor of Medicine" would, in a case of emergency or many other situations, render professional aid and assistance to the best of his ability without thought of his obligations incurred under his Hippocratic Oath. Such is not the situation here. This regulation enforces his services not voluntarily contracted for or perhaps not desired by the patient, yet compulsorily enforced upon him. To enforce the rule would enslave him. It is of course axiomatic that licensed physicians have no constitutional right to practice their profession in a hospital maintained by state or political subdivision. *Hayman v. City of Galveston*, 272 U.S. 414, 47 Sup. Ct. 363, 71 L. Ed. 714. It is likewise the general law that municipalities may regulate and control their hospitals and prescribe reasonable rules and regulations to be followed by physicians using the facilities. *Green v. City of St. Petersburg*, 154 Fla. 339, 17 No. 417; *Selden v. City of Stirling*, 316 Ill. App. 455, 45 N.E. 2d 329. For the general rule, see cases cited, 41 C.J.S., Hospitals, Sec. 5. Any public hospital having adopted reasonable rules and regulations governing the practice of medicine or surgery cannot arbitrarily preclude a regularly licensed physician or surgeon the right to practice in such hospital, so long as such surgeon or physician stays within the law. *Henderson v. Knoxville*, 9 S.W. 2d 697, 60 A.L.R. 652.

The provisions of section 17-349, *supra*, expressly confer upon a paying patient in a county hospital the privilege of employing a private physician without expense to the county, and such physician shall be permitted the necessary use of the hospital facilities and equipment. This express provision destroys any implication of a power to exclude physicians from the use of the county hospital except for a nonadherence to reasonable rules and regulations. We are without professional knowledge as to what might be encompassed within the definition of "reasonable rules and regulations". The managements of all modern hospitals require physicians and surgeons to keep thorough and clinical reports concerning their patients and their treatment, which become records of the hospital. Wards are provided for obstetrical cases; contagious cases and operative cases. Additional rules provide for numerous hygienic precautions. The reading of the cases indicates that hospitals have adopted rules denying the young and inexperienced surgeons the right to perform certain operations in the hospital except under the guidance or observation of an experienced practitioner. The rules and regulations just referred to all have reference to an orderly management of the hospital and in most instances are made for the protection of patients. Such rules and regulations appear to be reasonable and no doctor could be heard to complain for having to comply therewith. But the regulation under consideration goes beyond and transcends the ordinary and commonplace regulations and invades the personal liberty and contractual rights of both the patient and the physician. To accede to the rule by what virtually amounts to compulsion would be repulsive and beneath the dignity of a professional man.

"* * * Physicians are not public servants who are bound to serve all who seek them, as are innkeepers, common carriers, and the like. * * *" 41 Am Jur., Physicians and Surgeons, Sec. 4.

"A physician is under no obligation to engage in practice or to accept professional employment, but when the professional services of a physician are accepted by another person for the purpose of medical or surgical treatment, the relation of physician and patient is created. The relation is a consensual one wherein the patient knowingly seeks the assistance of the physician and the

physician knowingly accepts him as a patient. * * *" 41 Am. Jur., Physicians and Surgeons, Sec. 71.

In view of the circumstances surrounding this case it is apparent that petitioners had no plain, speedy and adequate remedy to protect their rights and to fulfill their obligations as physicians in the treatment of the private patients who might be regularly admitted as paying patients. Respondents suggest that a declaratory judgment and an appeal in the event of an adverse judgment would have afforded adequate relief. With this contention we cannot concur.

We therefore hold that the resolution was unconstitutional; that all action taken under it is and was of no effect. Having reached this conclusion, it is by way of anti-climax to point out that the resolution provided no method for review and that the action of the board in finding the petitioners guilty of violating the rule without accusation, notice or trial, finds no basis under our system of law requiring due process where substantial rights of citizens are infringed upon or destroyed.

The judgment quashing the writ and dissolving the stay is reversed, and the trial court is instructed to enter judgment reinstituting the *desist* order.

Judgment reversed.

R. C. STANFORD

Justice

CONCURRING:

LEVI S. UDALL

Chief Justice

ARTHUR T. LaPRADE

Justice

PHELPS and De CONCINI, Justices (Specially Concurring):

We concur in the result reached in this case to the effect that the judgment of the trial court quashing the writ of certiorari and dissolving the stay must be reversed but we heartily disagree with the ground assigned in the majority opinion for its reversal, to wit, that the resolution passed by the board of supervisors is unconstitutional.

The ground upon which the judgment of the lower court should be reversed, in our opinion, is that in the finding of the board; that the appellants had violate resolution No. 111 previously passed by it; and in its order prohibiting appellants from further use of the facilities of the county hospital the board was in the exercise

of a judicial function. It was therefore without jurisdiction to render the judgment complained of until it had given appellants an opportunity to be heard and had presented to it evidence sustaining the finding that appellants refused to assist the county doctor professionally in the treatment of patients or in the performance of operations upon patients confined in the county hospital.

Let us pause here to observe that the word *professionally* has no such connotation as indicated by the majority opinion. It would not only not be professional but it would be highly unprofessional for a physician to assist in the performance of an operation which he believed to be unnecessary or unwise to perform at that time.

As we view the matter there is no basis whatever for holding that resolution No. 111 is unconstitutional. No provision of the constitution is involved and no effort has been made to point to any specific provision thereof which the resolution violates.

All of the powers of the board of supervisors were granted to it by the legislature and it has only such powers as have been expressly, or by necessary implication, delegated to it. Section 17-305 (5), A.C.A. 1939, relating to the construction and maintenance of hospitals for the indigent sick and the dependent poor is set out in full in the majority opinion. Section 17-348, A.C.A. 1939, provides:

"No person other than an indigent shall receive public aid, or be admitted into any home or hospital the expenses of which are paid by the county, and any contractor or person having charge of any such home or hospital who knowingly receives into the same, for medical attention or subsistence, any person other than an indigent, shall be guilty of a misdemeanor. The board may admit into such hospital for hospital care, medical or surgical attention, any person other than an indigent who will pay, in part or in whole, for such hospital care, medical and surgical attention, *under rules and regulations prescribed by the board.*" (Emphasis supplied.)

The material portions of section 17-404, A.C.A. 1939, are set out in the majority opinion and will not be here repeated. This section contains at the end thereof identically the same language as section 17-348, *supra*, relative to the admis-

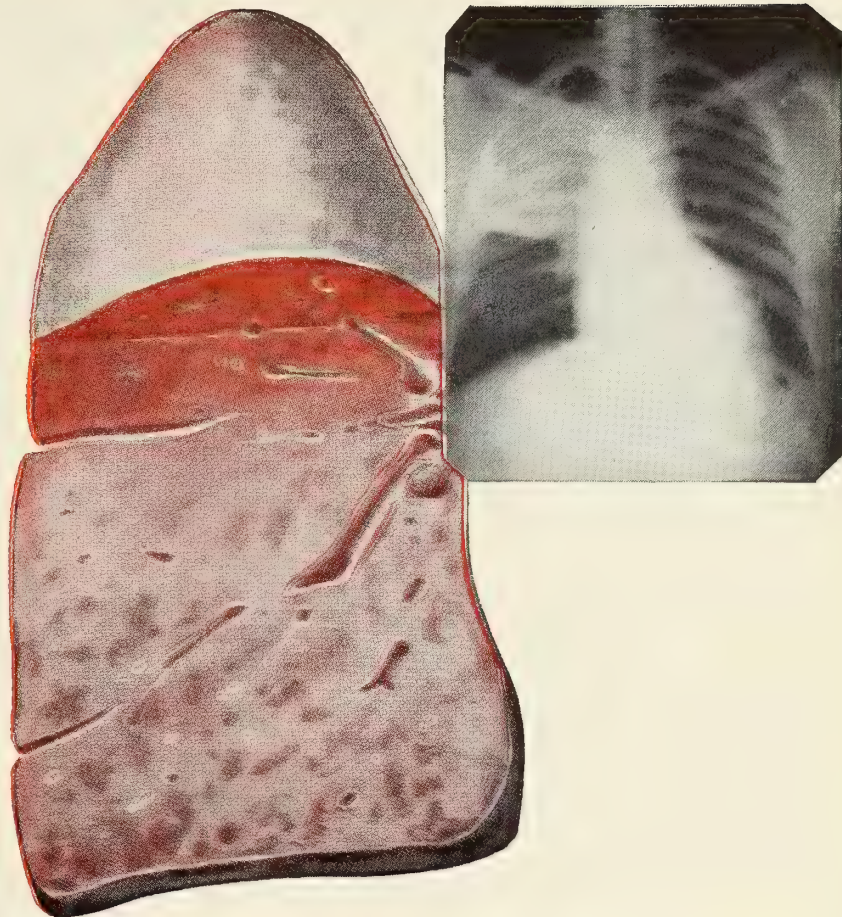
sion to the hospital of persons other than indigent patients and reiterates the power of the board to adopt rules and regulations governing their admission and treatment. Section 17-349 provides in part as follows:

"* * * Any person other than an indigent who has been admitted to the county hospital, may employ, without expense to the county, a physician or nurse who shall be permitted the necessary use of the hospital facilities and equipment. The admission of a paying patient shall not be the inconvenience of any indigent patient and an indigent patient shall receive the same care and treatment accorded to pay patients."

We believe all of the members of the court agree that in adopting resolution No. 111 the board of supervisors was acting in a legislative capacity. This being true we are neither concerned nor have we the authority to question either the reasonableness or the wisdom of the board in adopting it. These matters rest exclusively with the board. The authority of this court is limited solely to the determination of the question of whether the board in passing resolution No. 111 acted within the power and jurisdiction vested in it by the provisions of law above quoted. We think it did.

The board of supervisors is charged by the above law with the duty of providing for the care and maintenance of the indigent sick and the dependent poor of Mohave County and were empowered to build and maintain a hospital for that purpose. The power to maintain carries with it by implication the power to supervise and control it. The hospital is the property of Mohave County. Except in emergency cases when immediate hospitalization or medical care is necessary for the preservation of life or limb no person is allowed to be admitted to such hospital without first applying to the board of supervisors for such admission and it is made a misdemeanor for any person in charge of the hospital to admit a person for hospital care, medical attention and subsistence without the consent of the board. Sections 17-348 and 17-404, *supra*, provide that the board may admit paying patients *under rules and regulations prescribed by it*. The language used in these sections amounts to an express grant of power to adopt rules and regulations governing the admission of paying patients.

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Potterfield, T. G., and Starkweather, G. A.:
J. Philadelphia General Hosp. 2:6 (Jan.) 1951

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none of the characteristics of a public service corporation and is not bound to accept for treatment anyone who applies therefor. The statute expressly gives to the board the power to reject paying patients. In our view of the matter the clause "may admit into such hospital" is purely permissive and when considered together with the entire act cannot under any circumstances be construed to mean "must admit * * *".

Resolution No. 111 was adopted in accordance with and in the light of the above statute. Provision is made in said resolution for appellants to use the facilities of the hospital for any patient they then had in the hospital. The board has the right as above stated to refuse to admit to the hospital for treatment any and all patients other than indigent.

Upon what right then does the claim of appellants to the use of the hospital and its equipment rest? They have no property right in the hospital or in its equipment or its facilities. The right to practice medicine is not a property right. Appellants are merely licensees as medical practitioners and their licenses may be revoked at any time for cause. Therefore they cannot claim that any property right of theirs has been taken from them, in denying to them the use of the hospital facilities. The mere fact that they are licensed to practice medicine in

the state and are engaged in the practice thereof in Mohave County does not of itself give them any legal right to arbitrarily use the county hospital and its facilities in the furtherance of their practice. It cannot logically be said therefore that the regulation adopted by the board violated any legal rights of appellants. The board in adopting such regulation was acting within the express powers granted it by the legislature.

For this court to hold that the board may not adopt regulation No. 111 relating to the proper conduct and control of the county hospital for the purposes for which it was built and is maintained amounts to a mandate that the board of supervisors must abdicate its powers and authority to manage and control the hospital property of Mohave County, and by judicial fiat turns its management and control over to appellants including the power to dictate the appointment of the county physician of that county. It amounts to the taking of property without due process of law in violation of both the state and Federal Constitution.

M. T. PHELPS
Justice

EVO DeCONCINI
Justice

(Decided Apr. 23, 1951)

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MEDICAL CARE RELATIVELY CHEAPER THAN IN 1935-39

The American Medical Association reported that the price of medical care, including drugs, hospital room rates and physician and dental services, was relatively 14 per cent cheaper in 1950 than during 1935-39.

This was revealed in the Consumers' Price Index, compiled by the U. S. Bureau of Labor Statistics.

The Bureau's Index indicated a 72 per cent rise in the cost of living since the 1935-39 base period while, at the same time, showing that medical care prices rose only 48 per cent.

The increase for food, the Index showed, was 104 per cent; apparel 88 per cent; rent 31 per cent; fuel, electricity and refrigeration 41 per cent; house furnishings 90 per cent; and 57 per cent for the items which the Bureau of Labor Statistics classified as miscellaneous. Only two of these items—rents, and fuel, electricity and refrigeration—rose less rapidly than medical care prices.

The 72 per cent rise in the cost of living as compared with only a 48 per cent rise in medical care prices indicates that for every \$1 paid for goods and services generally in 1935-39, the 1950 consumer had to pay \$1.72. On the other hand, the medical care purchased for \$1 in 1935-39 cost only \$1.48 in 1950.

An analysis of the Index discloses further that a dollar in 1950 could buy 68 cents worth of medical care but only 58 cents worth of all goods and services, or 86 per cent as much. The 1950 purchasing power of the dollar was 86 per cent as high in terms of goods and services, generally, as it was in terms of medical care prices only. Thus, in terms of the purchasing power of the 1950 dollar, medical care was relatively 14 per cent cheaper than in 1935-39.

Physicians' fees, according to the Index, rose 40 per cent or only a little more than half as rapidly as the entire cost of living, which rose 72 per cent.

Only hospital room rates, which increased 135 per cent, have risen faster than the entire Consumers' Price Index.

"The high hospital rates," an A.M.A. study of the Consumers' Price Index said, "reflects the fact that hospitals are singularly exposed to the forces of inflation."

Commenting on the relatively cheaper medical care prices today, Dr. John W. Cline, San

Francisco, president of the A.M.A., said that "physicians recognize that the cost of medical care, especially hospital care, is a serious budget item for many persons. Therefore, the doctors are strongly supporting various voluntary prepayment insurance plans to help meet these costs."

"The fact is, however," Dr. Cline continued, "that, as shown by official government statistics, medical care prices today, as compared with the prices of all goods and services, are relatively less than they were 15 years ago."

AMERICAN COLLEGE OF PHYSICIANS

A regional meeting of the American College of Physicians was held in Phoenix, Arizona, Saturday, September 29, 1951, at Hotel Westward Ho. Approximately 100 members of the medical profession from Arizona and New Mexico were in attendance.

Dr. Dwight L. Wilbur, Clinical Professor of Medicine at Stanford University School of Medicine in California, discussed causes of failure in the medical treatment of peptic ulcer. He stated that if a patient with peptic ulcer under controlled conditions in the hospital does not become symptom free within a very few days, one must look for some complication such as a perforating type of ulcer, obstruction, or some other disease that is giving pain rather than the ulcer, such as gall bladder or pancreatic disease. He declared that the cause of stomach ulcer still baffles the medical profession; further, that "physicians now are no nearer a solution to the stomach ulcer problem than they were 50 years ago." X-ray now makes diagnosis more positive in the nervous type of individual who is more susceptible to ulcers. Physicians are presently deemphasizing surgery and returning to diet and medical treatment for stomach ulcers.

Dr. Roy Hewitt of Tucson presented a paper on intermittent positive-pressure breathing therapy. He discussed the physiology of respiration and the fact that some patients with dyspnea will blow off enough carbon dioxide to decrease their respiratory stimulations. Administering oxygen to these patients will make them worse and the respirations will decrease still more. He gave instances of beneficial results in some patients with emphysema, some with asthma and some post-operative patients

who fail to breathe and raise sputum properly.

Dr. Morris Deitchman of the Phoenix Regional Veterans Administration Hospital gave a paper on direct venous pressure in chronic right heart disease. He stated that chronic right heart failure can be diagnosed earlier by taking a venous pressure reading and changes can be brought out by the simple maneuver of pressure over the liver.

Dr. Israel Wolger of the Veterans Hospital at Prescott discussed carcinoma of the lung in patients with chronic pulmonary diseases. He cited several instances of carcinoma of the lung in patients with chronic emphysema, bronchiectasis and tuberculosis. He emphasized the fact that patients can have a malignancy in association with their previous disease.

Dr. Joseph Bank of Phoenix gave a paper on primary carcinoma of the liver. Diagnosis of this disease is very difficult and is usually made at postmortem unless one thinks of this condition. Four cases of this disease were presented.

FOURTH ANNUAL PUBLIC RELATIONS CONFERENCE

Your Executive Secretary was privileged to attend the Fourth Annual Public Relations Conference sponsored by the American Medical Association, held in Hotel Biltmore, Los Angeles, December 2 and 3, 1951. Also in attendance were Frank J. Milloy, M. D., Secretary, and William B. Steen, M. D., Chairman of the Board of Public Relations, both of this Association; Dermont W. Melick, M. D., President, Leslie B. Smith, M. D., President-Elect, Frederick G. Mitten, Executive Secretary, and Miss Alma Alkire, representatives of the Maricopa County Medical Society.

On Sunday, December 2, John W. Cline, M. D. of San Francisco, President of the American Medical Association, delivered the address of welcome and introduced Louis H. Bauer, M. D. of Hempstead, New York, President-Elect, who delivered the keynote address: "Working Together in '52." He urged all physicians to unite and work together in an effort to "restore what has been destroyed of our individual liberty." He continued: "One trouble today in the United States is the lack of civic responsibility of many of our citizens. Our duties as doctors are great, but our duties as citizens are even greater. This country has been built on a spirit of competition and free enterprise. During recent years there

has been a studied attempt to diminish the importance of self-reliance or the desire to improve one's lot and substitute instead a dependence on government. America has become a bureaucracy, ruled largely by administrative law." Physicians must accept their civic responsibilities and "lead the way back to freedom," enlisting the support of other organizations and individuals. "We have a minority government because on the last national election only 47 per cent of those entitled to vote actually voted. Physicians must join in the fight for Americanism."

The afternoon session was presided over by Gunnar Gundersen, M. D. of La Crosse, Wisconsin, Chairman of the Executive Committee of the Board of Trustees of the American Medical Association.

Ernest Dichter, Ph. D. of New York, Psychological Consultant, addressed the group taking for his subject: "A Psychologist Studies Medical Care." Dr. Dichter recently completed an intensive medical care study in California. He stated: "We should not lose track of the emotional element involved in the high cost of sickness. People do not complain about the high cost of television sets because they don't have any animosity toward TV. Everyone dislikes sickness. He cited the importance of the psychological element in maintaining the doctor-patient relationship. Pointing to the conflict between idealism as against realism, he stated people have become more mature and are reading considerably more today. They want to know. They consult the doctor sooner and more frequently. Patients want to know the why and wherefore. There seems to be a lack of explanation regarding the high cost of medical and hospital care, and while it may be impossible to substantiate such costs through facts, the public's emotions must be combated in their desire for enlightenment. The doctor should state individually and publicly his realistic idealism. That certain resentment against doctors must be attacked patiently. Public resistance must be removed. The doctor should recognize that the world has changed and continues to change, and that medical practice is part of this world.

Edgar A. Schuler, Ph. D. of Detroit, member of the Department of Sociology at Wayne University, reported on a survey of medical care opinion in the Toledo, Ohio area, conducted by the Health Information Foundation of New York.

Lawrence W. Rember of Chicago, Director of



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SEARLE RESEARCH IN THE SERVICE OF MEDICINE

Field Service, AMA, Department of Public Relations, selected as his topic, "An Urban-Rural Opinion Test Tube", reporting on a recently completed survey about medical care and doctors in a southern Illinois community.

Joseph D. McCarthy, M. D. of Omaha, Chairman of the American Medical Association, Council on Medical Services, presided over a panel discussion on "The Cost Factor In Everyday Practice" during the Monday morning session of December 3. "Fees Should Be No Mystery" was the subject presented by Harlan A. English, M.D. of Danville, Illinois, Committee on Rural Medical Service, Illinois State Medical Society. The three most frequent questions asked by the patient of the doctor following diagnosis are: "Doc" can this be cured? How long will it take? How much will it cost? He urged all doctors to take time to discuss costs during the patient's first visit, particularly where surgery is indicated. It was recommended that it would be better to cancel a charge than reduce a fee in deserving situations.

Cyrus W. Anderson, M. D. of Denver, Chairman of the Board of Trustees of the Colorado Medical Society, had for his topic: "Explaining Those 'Other' Medical Expenses." Reviewing medical costs in 1871 when office calls were \$3.00 and prescriptions \$2.00, with those of today, in comparison with increased costs for labor and other commodities, he pointed the need for a more detailed explanation to the patient of hospital costs; tests, routinely or otherwise required; cost of expensive drugs and benefits expected through their use; consultation and anesthetic fees when indicated; and recommended that all bills be itemized. He urged establishment of a "code of cooperation" with the doctors similar to that in practice in Colorado with the press.

Dr. E. E. Wadsworth of Alhambra, California, read the paper prepared by Dr. Stanley R. Truman of Ventura, California, Past President of the American Academy of General Practice (who was ill) entitled: "Time is Money for Your Patients, Too."

A second panel during the morning session on "Medical Society Solutions to the Cost Problem" was presented. Stanley R. Mauck of Columbus, Ohio presented the "PR Factor in Collecting Bills"; Earl W. Mericle, M. D. of Indianapolis, Chairman, Public Relations Committee, Indiana State Medical Association, spoke on "Your Pa-

tient and His BIG Bills"; and Joseph F. Donovan of San Jose, California, Executive Secretary, Santa Clara County Medical Society discussed: "The 'Regardless of Ability to Pay' Idea."

Possibly the highlight of this day's session was the address delivered by Lewis A. Alesen, M. D. of Los Angeles, President-Elect, California Medical Association. He warned there is danger ahead in the philosophy that "capitalism is just a temporary way station on the road to socialism." He vigorously pointed out the responsibility of American physicians to reverse the trend toward socialism.

"Joining Forces With Other Groups", was the theme of the afternoon panel under the Chairmanship of Harvey Sethman of Denver, Chairman, Advisory Committee to the Department of Public Relations of AMA. Ernest B. Howard, M. D. of Chicago, Assistant Secretary of AMA, spoke on "Representing Physicians on the National Level"; Willis H. Huron, M. D. of Iron Mountain, Michigan, Past Councilor of the Michigan State Medical Society, discussed "State-Wide Organizations and the Medical Society"; and George Schwartz, M.D. of New York, Committee on Public Relations, Bronx County Medical Society, reviewed "The Doctor in Community Affairs."

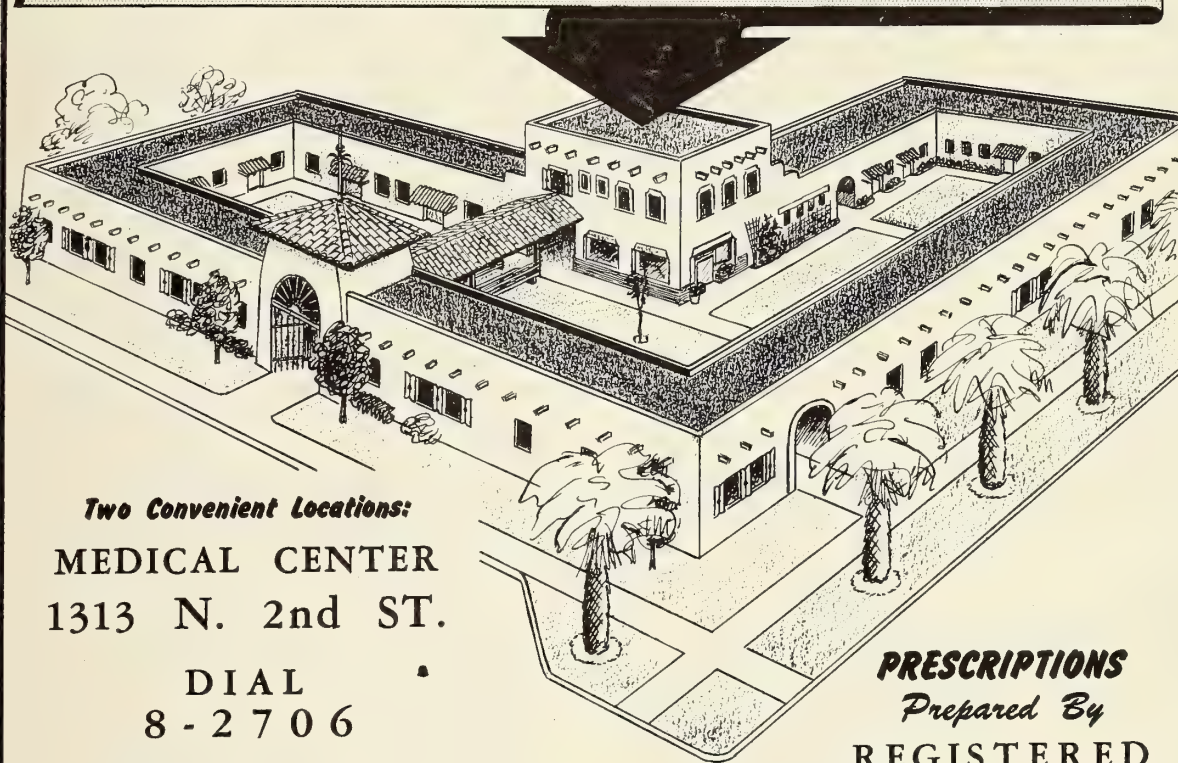
Leo E. Brown of Chicago, AMA, Director of Public Relations, as Chairman of the panel, "Where Do We Go From Here?", reviewed "Your AMA's 1952 PR Program"; Joseph E. Mott, M. D. of Patterson, New Jersey, Sub-Committee on Public Relations, Medical Society of New Jersey, spoke on "Public Relations Goals for State Societies"; Fred G. Mitten, Phoenix, Arizona, Executive Secretary, Maricopa County Medical Society reviewed, "What the County Society Can Do." He made a splendid presentation which was well received. Charles R. Henry, M. D. of Little Rock, Arkansas, President, Arkansas State Medical Society discussed, "The Individual Physician's Role."

More than 450 persons were registered for the two day conference. Most significant is the fact that today in excess of 77,000,000 people in the United States have some form of prepaid health insurance. The voluntary way is the American way, and as we continue to "pull together through '52", the battle against socialism in this great country of ours will be more readily achieved.

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1951 ARIZONA GOVERNOR'S CONFERENCE ON CHILDREN AND YOUTH

The Governor's Conference on Children and Youth was held in Phoenix, November 9-10 at Phoenix College. The Conference's eight hundred delegates included representatives from many civic and welfare organizations, and outstanding leaders from various youth groups. The Arizona Medical Auxiliary was represented by the following delegates:—Mrs. George S. Enfield, State; Mrs. T. C. Harper, Globe; Mrs. T. W. Woodman, Mrs. Dwight Porter and Mrs. Jesse Hamer, Maricopa; Mrs. Joseph M. Kinade, Pima; and Mrs. Harry T. Southworth, Yavapai.

Friday's sessions included registration, panel discussions and two general sessions. The opening General Session presented a resume of the White House Conferences and talks on "What Youth Expects of This Conference." The evening Session was high-lighted by Governor Howard Pyle's "Keynote Address" followed by W. Cleon Skousen's discussion of "Teen-Age Troubles". Saturday's activities included Workshop Sessions and closed with a final Plenary Session at which findings and recommendations of the Workshops were presented for adoption.

Topics discussed in the Workshops were:—

1. The Role of Formal Education in the Development of Youth.
2. Recreation and Leisure Time of Youth.
3. Toward an Improved Home and Religious Environment.
4. The Law and The Child.
5. Children in Minority Groups.
6. Mental and Physical Health of the Child.

In the following paragraphs is given a condensation of a few of the seventy-five recommendations made by this conference. Particular attention has been paid to those recommendations which have a direct bearing on the problems as stated in the Survey Report of Arizona Children and Youth (conducted by the Arizona Council on Children and Youth.) A copy of the Survey and of all recommendations adopted may be obtained from Mr. John F. Allanson, Executive Secretary of the Arizona Council on Children and Youth, State Office Building, Phoe-

nix, Arizona. There is a charge of fifty cents to cover cost of printing and mailing.

FINDINGS OF THE SURVEY

I. EDUCATION

Present Arizona education laws only require school attendance for youth under the age of sixteen, or fourteen (with a few simple and easily met specifications), or until the child has completed the eighth grade. The present national trend among the states is to raise the required age limits to at least sixteen years of age and with as few exceptions as possible.

The average classroom load obtained from figures given was 33. This was due to many districts reporting low numbers which counter-balanced the crowded conditions in the city schools where classes were staggered to meet the needs.

II. RECREATION AND LEISURE

Six counties reported tax supported programs in 1949. Most are recent, since only Maricopa and Pima counties were receiving tax support prior to 1948.

Private volunteer agencies operate in many counties. Are limited by so few available volunteer leaders.

It was noted in Maricopa County that over 91% of the juvenile cases were listed as belonging to no youth organization of any kind.

The problem of unemployed youth, who cannot obtain employment has grown more significant as a contributing factor to juvenile delinquency.

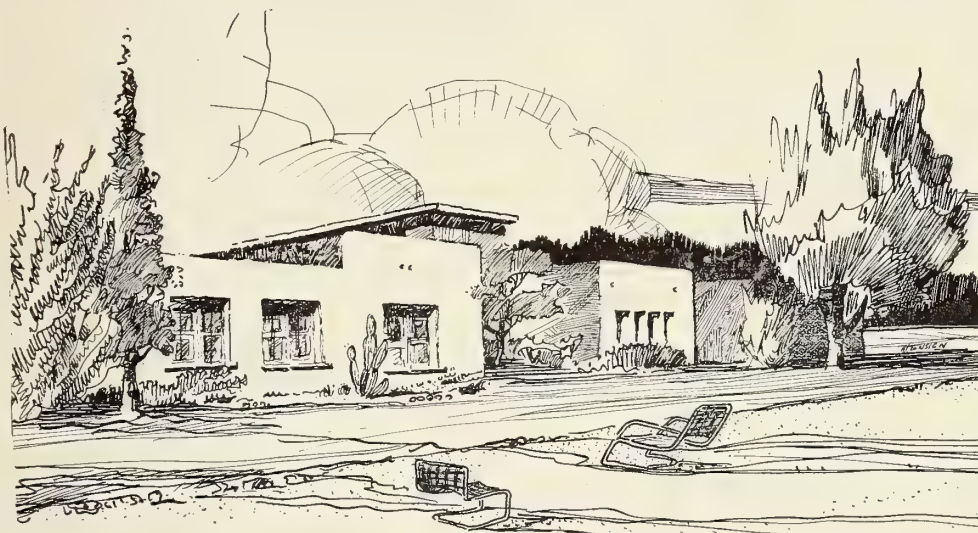
III. HOME AND RELIGIOUS ENVIRONMENT

Reports estimated that as low as 18% to 25% of the total children and youth groups in some counties were in attendance at a Sunday School. Family participation in church programs were checked and figures ranged from 40% to 61% of parents of children in Sunday School, who participate to some degree in church programs.

It is likewise noteworthy that a reliable law enforcement agency indicated that "Most of the cases listed as 'Juveniles' who specified themselves as having no religious affiliations, have usually been found to be the real 'Juvenile Delinquents' and are the ones responsible for most of the serious crimes committed by youth."

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IV. THE LAW AND THE CHILD

In regard to serious crimes, narcotic addiction among youth was felt to be one of the state's greatest criminal problems with juveniles, not only in its own respect, but perhaps even more so in its role as contributing factor to other crimes.

It was generally agreed that one of the most serious problems with children today both in Arizona and nationally, is the lack of moral and religious training (particularly in the home). Because of the lack of genuine interest and good examples on the part of many of our homes and some of our churches and schools, an increasing number of our youth has come to rely on such things as cheap magazines and movies as examples to follow in their moral and religious training and education.

Arizona has no law requiring a license for day care. In 1948 the city of Phoenix passed an ordinance requiring that day care centers and nurseries handling five or more children be inspected for health and safety. Additional control and supervision of such care is needed for the protection of pre-school children in the state.

According to police records, the "Danger Age" of youth in Arizona ranges between 14 and 17 years of age. It is in this group that the greater majority of crimes committed by juveniles are found. The greatest number of violations had been on the following counts listed in order—traffic violations, petty larceny, malicious mischief, burglary, drunkenness, incorrigibles, run aways and morals.

The Arizona Youth Authority, created by an act of Legislature in the 1951 session, is capable of doing a very beneficial job in the rehabilitation of delinquents. Its function is "to provide and administer corrective and preventive training and treatment for persons committed to it." However, this agency was not provided funds to carry on its work, and therefore, has been seriously handicapped in carrying on an effective program.

V. CHILDREN IN MINORITY GROUPS

The law which demanded segregation of negro children through the eighth grade was repealed by the last legislature and now gives the local boards of education discretion as to segregation in elementary as well as secondary schools.

There is a law of miscegenation in Arizona which bars legal marriage between the races. Surveys indicate that where children are born of these illegal marriages they are the ones to suffer, as it is possible for the marriage to be annulled on these grounds.

Maricopa County reported that many jobs were closed to negroes because of color distinction rather than ability.

In Pima County the Mayor's Law Housing Committee revealed that 72% of the housing units in Tucson's worst slums were occupied by Spanish-American, 26% more by Negro. Housing conditions of the majority of negroes were acclaimed as substandard and, if they were economically able, they did not feel free to live in any part of town they choose.

During the past few years more Indians have been moving into the fringes of our communities from the reservations. Many counties felt that the problem of integrating the Indian people into our American way of life was becoming the major minority group problem, principally because more and more of them have left and are being encouraged to leave the isolation of the reservations.

VI. MENTAL AND PHYSICAL HEALTH OF CHILD

The 1950 estimate of Arizona's population under 15 years of age was approximately 243,000 or about 23% of the total state population.

There is a serious shortage of Doctors, Public Health Nurses, and Sanitariums in the State.

The national per capita legislative appropriation for public health is 63 cents, Arizona's appropriation is 19 cents per person.

Arizona's infant mortality rate last year was the second highest in the nation due to the high infant mortality among the Indians. Due to their low economic status they are forced into substandard living conditions which facilitated the spread of such diseases as diarrhea-enteritis, which is their particular enigma, and has contributed to their high infant mortality rate.

Arizona's death rate from Tuberculosis is three times national average. Percentage of tuberculosis in native-born is greater than in those from other states. There are no hospital facilities for non-Indian tubercular chil-

dren. There are only about 300 hospital or sanatoria beds available for over 10 thousand active tubercular cases in state.

There is very little being done in Mental Hygiene among children and youth in Arizona although the need for such service is great. The Children's Colony will be able to accept only a third of the cases submitted for entrance.

Only one county—Cochise—has an organized dental program for children.

—cover peddling and use of marijuana, as well as narcotics.

—make offenses a felony with strong penalties.

RECOMMENDATIONS OF THE CONFERENCE

I. EDUCATION

Schooling until the sixteenth year, "except for children of fifteen years who cannot profit by further available education."

Reduce class size and implement teaching to units of not over 25 children per teacher with compulsory age reduced to six years for starting school.

II. RECREATION AND LEISURE

We recommend a recreation and leisure time program for youth that has a definite purpose, and is creative, to include such activities as photography, art work, dancing and music.

That we should have programs of family recreation, but that families should begin to realize the necessity of their assuming more of the recreational load.

That more Youth Employment Services should be set up throughout the state as a means of giving youth gainful employment from which he gains character building benefit.

III. HOME AND RELIGIOUS ENVIRONMENT

That religion, as such, not be taught in the schools.

That there be released time in public schools for a program of religious instruction with this to be voluntarily supported and participated in by all churches.

That the family unit be re-established through a weekly family night in the home to increase the moral and spiritual values of our home life.

That in employing teachers, school adminis-

trators should require appointees to have an appreciation of religious values and that their teaching attitude uphold the importance and dignity of all religious faiths.

IV. THE LAW AND THE CHILD

That the state adopt a narcotics law which will—

—provide sufficient staff and adequate finances for enforcement.

That the Arizona Sexual Psychopathy Act (Child Molesting), as already drafted and presented at the 1948 and 1950 Sessions of the Legislature, be considered as a basis for final recommendation of the Governor's Conference on Children and Youth.

That civic and church groups conduct a program of adult education to accompany the efforts on the state level and secure local and state enforcement of laws concerning Children and Youth.

That a law requiring the licensing of all commercial homes and institutions providing group day care of children, providing for the setting up of minimum standards for such care and that the State Department of Public Welfare be the licensing agent.

That a complete study of the liquor laws be made with special attention to—

1. That section dealing with penalties as they now exist, be changed and that the following penalties be recommended—

a) upon the conviction of the owner of a liquor establishment, or anyone in his employ, of the sale of liquor to minors it shall be mandatory on the part of the commissioner to suspend said license for a minimum of 30 days and a maximum of 90 days.

b) upon the conviction a second time it shall become mandatory that said liquor license shall be revoked permanently and said licensee shall never be given the privilege of owning or operating any type of liquor establishment in the State of Arizona.

Recommend support of the Youth Authority Act and urge its activation, including appropriations.

V. CHILDREN IN MINORITY GROUPS

Complete integration of students and faculty,

instead of segregation, in schools of Arizona.

All laws of Arizona which bar the legal marriage of people of different races be abolished because of the detrimental effect on children and youth.

Legislation be enacted for fair employment practices in view of the effect of restricted employment upon the personality development of children and youth.

In order to insure the welfare of all children and youth good housing should be integrated and that maximum emphasis be placed on maintaining standards of health, comfort and decency in both private and public housing and that the standards be made available to people regardless of race, color or creed.

Resolution—presented by Thomas A. Segundo Papago Tribal Council Chairman.

Whereas, the State of Arizona does not provide care for Indian Crippled Children and

Whereas, the Medical services of the Bureau of Indian Affairs is not in a position to handle a program of this size, and

Whereas, the Federal Funds are being denied the State of Arizona because the State discriminates against crippled Indian children

Whereas, the Indian crippled children who are being denied corrective medical service are a potential financial liability to the State during the coming years,

Therefore, Be It Resolved that the Arizona Governor's Conference on Children and Youth recommend to the Governor and the State Agency administering the services for crippled Indian children on the same basis as all other crippled children in Arizona.

VI. MENTAL AND PHYSICAL HEALTH OF CHILD

That we extend to more areas the Well-Baby Clinics including pre-natal, post-natal and premature baby care as well as for young children.

That appropriations be increased for personnel to carry out our present health laws.

That Congress transfer Indian Medical Service from the Bureau of Indian Affairs to the United States Public Health Service, thus bringing up the appropriation on the State level and bringing the care of Indian children under State Public Health supervision.

Since tuberculosis is one of the greatest killers of young people we recommend that a definite program of tuberculosis control be formulated

by the State Department of Health and others interested and be presented to the legislature for implementation.

That colleges be encouraged to provide workshops on mental health and that the public schools be asked to adopt the general theme "Improving Mental Health" for one or more years.

That an office of Director of Dental Health be instituted in the State Department of Health. This officer shall be a member of the State Dept. of Health and be responsible to the State Director of Health.

Mrs. Dwight Porter
Mrs. George S. Enfield
Phoenix, Arizona

SOCIETY OF MEDICAL CONSULTANTS OF WORLD WAR II

W. Paul Holbrook, M. D. of Tucson was recently appointed a member of the Advisory Board of the Society of Medical Consultants of World War II. Other officers are: Dr. Grover C. Penberthy of Detroit, President, succeeding Dr. Garfield C. Duncan of Philadelphia; Dr. John Minor of Washington, Vice President; and Dr. Worth B. Daniels of Washington, Secretary.

Major General George E. Armstrong, Army Surgeon General, reported that another year will be required before efficacy of primaquine for malaria is fully determined.

PERSONAL NOTES

Dr. Kenneth C. Baker, Tucson, has returned from Chicago where he attended the 10th annual meeting of the Academy of Dermatology and Syphilology at the Palmer House.

—o—

Dr. R. Lee Foster attended the meeting of the Radiological Society of North America at Chicago December 7, 1951. He attended refresher courses in the following subjects: Radiotherapy, Roentgen Diagnosis of the Orthropathies, Diseases of the Chest in Infants and Children, Cancer of the Male Genital Tract, and The Chest in Industry.

Mrs. Foster accompanied him and on their return trip they visited relatives in Dr. Foster's boyhood home in Southern Illinois.

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